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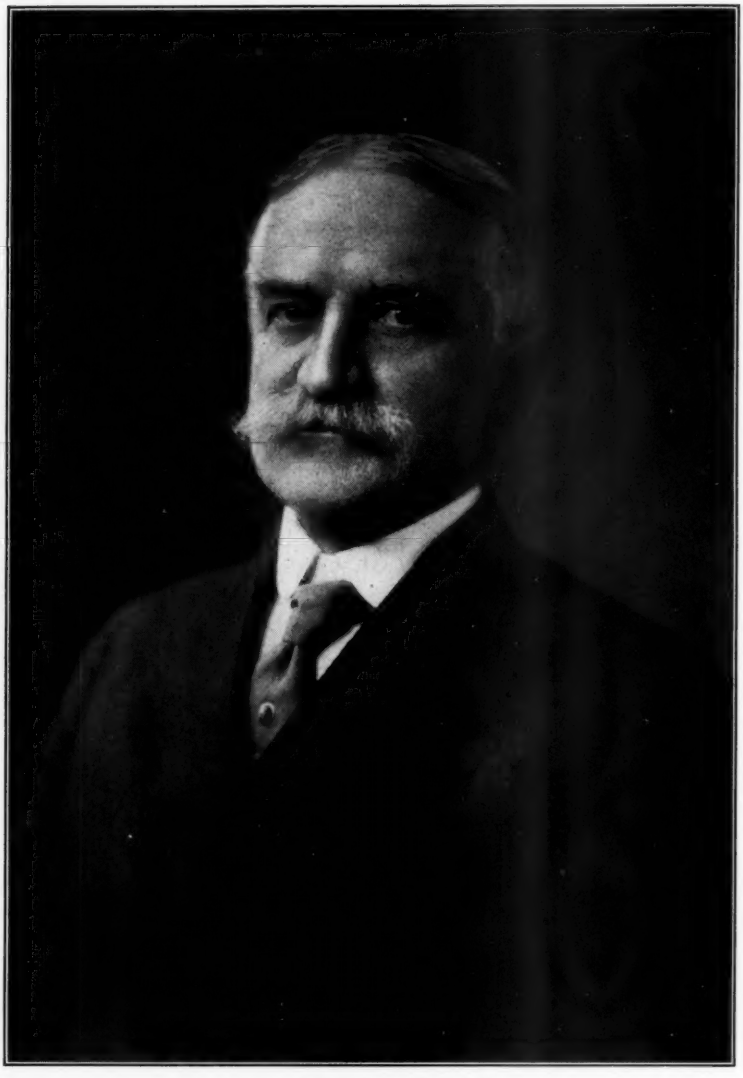

PROF. SAMUEL P. SADTLER,

Retiring Professor of Chemistry and Dean of the Department of Special Technical Instruction.

THE AMERICAN
JOURNAL OF PHARMACY

*JULY, 1916*

# SAMUEL P. SADTLER, PH.D., LL.D.

RETIRING PROFESSOR OF CHEMISTRY AND DEAN OF THE DEPARTMENT OF SPECIAL TECHNICAL INSTRUCTION.

Samuel Philip Sadtler, now emeritus professor of chemistry in the Philadelphia College of Pharmacy, was born at Pine Grove, Schuylkill County, Pa., July 18, 1847. His father, the late Rev. Dr. Benjamin Sadtler, was a Lutheran minister and served, in addition, for a period of ten years as president of Muhlenberg College, at Allentown, Pa. His early education was obtained at Easton, Pa., from the high school of which he graduated during his father's residence at that place, in 1862. The same year he entered Pennsylvania College, at Gettysburg, from which he graduated in 1867, his course having been interrupted during the year of the Battle of Gettysburg, in 1863.

In the fall of 1867 he went to the newly-established Lehigh University to begin his professional studies in chemistry, this choice being largely determined by the fact that his friend, Doctor Mayer, had been called there at that time as professor of physics. A year was spent here in the study of chemistry, physics, and mineralogy, when, having a desire for more extended opportunities, he went, in the fall of 1868, to Harvard University, where he entered the Lawrence Scientific School as an advanced student under Dr. Wolcott Gibbs, then the most distinguished chemist in America. After a year and a half spent here under Professor Gibbs in chemistry and Josiah P. Cooke in mineralogy he passed his examinations for the degree of Bachelor of Science in January, 1870, and a month later sailed for Germany, where he wished to complete his chemical studies.

After a year spent at the University of Göttingen, where he obtained the degree of Doctor of Philosophy in the spring of 1871,

and several months in travel, he returned in the summer of the same year to take up his life-work as a teacher of chemistry. From 1871 to 1874 he was professor of chemistry and physics in Pennsylvania College, from which he had graduated in 1867, and in the fall of 1874 he came to Philadelphia as professor of General and Organic Chemistry in the University of Pennsylvania. It was while holding this latter position that, in 1878, he was asked to relieve Prof. Robert Bridges, the venerable professor of chemistry in the Philadelphia College of Pharmacy, by taking part of his lecture work, and when, in the spring of 1879, Doctor Bridges was made emeritus professor of chemistry, Doctor Sadtler was elected as his successor. From that time to the present his interest in pharmacy has had a continuous growth, as is shown by his work as a teacher and his literary activity in that direction. The professorship at the University of Pennsylvania he relinquished in 1891, after seventeen years of service, and opened an office as consulting chemical expert, which he has since maintained.

Professor Sadtler has devoted much attention and study to the modern chemical processes of manufacture and to the field of Industrial Chemistry. He is recognized as one of the most prominent consulting chemists in America, and has been engaged as chemical expert in many of the most important patent suits of the last twenty-five years.

He has made a special study of petroleum and its products, and is widely known and consulted as an authority thereon. He was one of the two experts selected by the Citizens' Municipal Association and the Trades League of Philadelphia to investigate the subject of asphalts for street paving.

Professor Sadtler's first literary work was a "Handbook of Chemical Experimentation for Lecturers and Teachers," published in 1877. He was the American editor of the eighth edition of "Attfield's Chemistry," a text-book especially prepared for students of pharmacy in England and the United States. In 1880 he became associated with Dr. H. C. Wood and Prof. Joseph P. Remington in the revision of the United States Dispensatory, and still continues as the chemical editor of this great reference book. In 1891 he published the first edition of his "Industrial Organic Chemistry," which has since gone through four editions, having a wide circulation in this country and in England, and has appeared abroad in authorized German and Russian translations. In 1895 he published, jointly with his colleague,

Prof. Henry Trimble, the first edition of "Sadtler and Trimble's Pharmaceutical and Medical Chemistry." This has run through four editions, becoming known, after the death of Professor Trimble, as "Sadtler and Coblentz's Text-book." He attended the national conventions of 1890, 1900, and 1910 for the revision of the United States Pharmacopœia, as a delegate from the Philadelphia College of Pharmacy, and was elected by the conventions of 1900 and 1910 a member of the Standing Committee of Revision, in which capacity he is serving at present. He has contributed, in addition, many scientific papers to the chemical and pharmaceutical journals, and delivered many public addresses on chemical and technical subjects.

Professor Sadtler is an active member of numerous scientific societies, among which may be mentioned the American Philosophical Society, of which he was secretary from 1898 to 1902; the American Association for the Advancement of Science; the American Chemical Society, serving in the council of the latter for a number of years; the American Electrochemical Society, of which he was vice-president; the Chemical Societies of London and Berlin and the Society of Chemical Industry and The Franklin Institute, of which he was a manager for a number of years, and of which he is now emeritus professor of chemistry. As professor of chemistry in the latter institution he delivered for a number of years the chemical lectures in the popular course, and likewise presented to the members numerous advances in chemistry in special lectures. When the American Institute of Chemical Engineers was organized, eight years ago, he was unanimously elected its first president, and he has continued active in its management ever since, visiting all the great industrial centres of the country in attendance on its meetings. In this connection he has also come into close personal contact with the most prominent chemical manufacturers of the United States and Canada. Of distinctively pharmaceutical societies, he is a member of the American Pharmaceutical Association and the Pennsylvania State Pharmaceutical Association. He is also a member of the Chemists' Club, of New York, and of the University Club, the Engineers' Club, and the City Club, of Philadelphia.

In 1902, Pennsylvania College, at Gettysburg, Pa., honored him on the occasion of the thirty-fifth anniversary of his graduation by conferring on him the honorary degree of Doctor of Laws, and in 1912 the Philadelphia College of Pharmacy conferred the honorary degree of Master of Pharmacy.

Prof. Samuel P. Sadtler became an active member of the Philadelphia College of Pharmacy in 1879, and in the following year was elected as one of its trustees and continues as such to date.

He has served on many of the important committees of the college, and has been chairman of the Committee on Publication of the AMERICAN JOURNAL OF PHARMACY since 1895.

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## OPIUM ASSAY: COMPARISON OF THE METHODS OF THE UNITED STATES AND BRITISH PHARMACOPŒIAS.

By CARL E. SMITH.

It will be generally conceded that no method for the quantitative determination of morphine in opium has yet been published that is capable of the degree of accuracy highly desirable in a medium that serves as a basis for price adjustments of a drug as costly as opium. The assay methods of the pharmacopœias have been arranged and adapted primarily for the adjustment of doses, for which purpose they are reliable enough, with few exceptions. A fair degree of accuracy is all that can be expected in their application, since editors of pharmacopœias take the stand that pharmacopœial methods of testing should be simple enough to be used successfully by pharmacists having only limited practice and training in analysis. But simplification of analytical procedures often entails a sacrifice in precision of results, and this is particularly true of opium assays. Buyers and sellers of large quantities of opium, therefore, do not generally rely upon pharmacopœial assay methods to ascertain as closely as possible the morphine contents of this drug.

The method of the British Pharmacopœia of 1914 may be expected to have the same limitations as others of its kind. Nevertheless, it is of interest because it is one of the latest in this field having official sanction and, therefore, may be expected to embody, to some extent, such advances as have been made in recent years in this branch of analysis. In its present form it has not been in use long enough for many data concerning it to have accumulated, and the writer has not yet seen any reports of critical study that furnish a clue as to the degree of accuracy of which it is capable. Such data would be useful, also, in view of the prevailing differences of opinion in this country about the relative merits of lime methods, of which the British

is an example, and methods of the type originated by the late Dr. E. R. Squibb, as adopted by the U. S. P. in the seventh and eighth revisions.

The process of the eighth revision was held by Dr. Squibb to yield results a little too low, as he was able to obtain in actual manufacture somewhat larger yields of morphine than assays of the opium by that method indicated it to contain. It should be considered, however, that when Dr. Squibb made that statement medicinal morphine and its compounds contained notable proportions of unsuspected impurities that would not now be tolerated and which appreciably increased manufacturing yields. Dr. A. R. L. Dohme [1] considers the U. S. P. method to give *much too low* results. A manufacturer of opium alkaloids, who bases his conclusion on manufacturing yields by up-to-date methods, has stated to the present writer his conviction that the process gives *too high* results. These are only a few examples of the many differences of view that tend to throw doubt upon the reliability of the U. S. P. method.

The B. P. method, not being accessible to many American readers as yet, is copied here in full:

OPIUM ASSAY METHOD OF THE BRITISH PHARMACOPŒIA OF 1914.

| | |
|---|---|
| Opium, in No. 50 powder, dried at 60° | 8 grammes |
| Calcium Hydroxide, freshly prepared | 2 grammes |
| Ammonium Chloride | 2 grammes |
| Alcohol (90 per cent.), Ether, Distilled Water | of each a sufficient quantity |

"Triturate together the Opium, *calcium hydroxide*, and 20 millilitres of *water*, in a mortar until a uniform mixture results; add 60 millilitres of *water* and stir occasionally during half an hour. To 51 milliliters of the filtered liquid (representing 5 grammes of Opium) in a convenient vessel add 5 millilitres of *alcohol* (90 per cent.), and 25 millilitres of *ether;* shake the mixture; add the *ammonium chloride*, shake well and frequently during half an hour; set aside for 12 hours for the morphine to separate. Counterbalance two small filters; place one within the other in a small funnel in such a way that the triple fold of the inner filter shall be superposed upon the single fold of the outer filter; wet them with ether; remove the ethereal layer of the liquid in the vessel as completely as possible by means of a small pipette, transferring the liquid to the filter; rinse the vessel with 10 millilitres of *ether*, again transferring the ethereal layer, by means of the pipette, to the filter; wash the

[1] *Jour. Am. Phar. Ass.*, 1915, vol. 4, p. 85.

filter with a total of 5 millilitres of *ether*, added slowly and in portions. Let the filter dry in the air and pour upon it the contents of the vessel in portions, in such a way as to transfer the granular crystalline morphine as completely as possible to the filter. When all the liquid has passed through, wash the remainder of the morphine from the vessel with *morphinated water* until the whole has been removed. Wash the crystals with *morphinated water* until the washings are free from colour, allow the filter to drain, and dry it, first at 60° and finally, for two hours, at 115°. Weigh the crystals in the inner filter, counterbalancing by the outer filter. Dissolve 0.2 gramme of the crystals in 10 millilitres of *N/10 solution of sulphuric acid*, and titrate back with *N/10 solution of sodium hydroxide, solution of methyl orange* being used as indicator. Each millilitre of the acid neutralised by the alkaloid corresponds to 0.0285 gramme of pure anhydrous morphine. The weight of pure anhydrous morphine obtained, as indicated by the titration, plus 0.051 gramme, the average loss of morphine during the process, together amount to 0.5 gramme, representing in 100 grammes of the dry powdered Opium 10 grammes of morphine, calculated as anhydrous. *Limit of error* 0.5 gramme in excess or defect."

"Morphinated Water, prepared by digesting pure Morphine in Chloroform Water for seven days at a temperature of 15.5°, shaking occasionally so as to obtain a saturated solution of the alkaloid, and filtering from the undissolved morphine."

### Comparative Assays.

The assays given below are of a specimen of powdered opium bearing the label of Merck & Co., and stated to contain the U. S. P. percentage of morphine.

To facilitate comparison, the results in this paper are in all cases stated as hydrated morphine.

| | Per Cent. of Morphine Found. | |
|---|---|---|
| | U.S.P., 8th Rev. | B.P., 1914 |
| | 12.19 | 12.37 |
| | 12.10 | 12.48 |
| | 12.23 | 12.33 |
| | 12.21 | 12.34 |
| Mean result ..... | 12.18 | 12.38 |

It is seen that with this particular sample no marked differences in results were obtained by the two methods, though a tendency toward somewhat higher figures are shown by the B. P. method. But it would not be safe to conclude that a similar concordance of results by the two methods would be obtained, or that the British process would consistently give a little higher results with any and all kinds of opium of abnormal composition. The methods differ radically in

their means of arriving at the end, and opium from different sources varies much in the proportions of constituents that contaminate the precipitated alkaloid and probably, to some extent, affect its solubility in the precipitate liquors.

The U. S. P. assumes that those impurities in the morphine which are not excluded by the lime water correction compensate with sufficient accuracy for the loss of morphine in the precipitate liquors. The proportion of such impurities, however, is subject to a wide variation. In a considerable number of assays of various kinds of opium by the U. S. P. method the writer has found in the morphine, besides matter insoluble in lime water, from 5 to 11 per cent. of other impurities—much too great a variation to be counterbalanced with any degree of certainty by the loss of morphine in liquors.

Attention should be called here to the rather vague directions in the U. S. P. pertaining to washing the crystals on the filter with the alcohol solution of morphine. It is important, though not stated, that washing with this solution be continued until the washings are practically colorless. This requires 10 Cc. *or more.* Failure to do this may cause the crystals to retain a much larger quantity of alcohol-soluble impurities than is allowable. Some years ago the writer was asked to investigate the causes of discrepancies in assays of a number of lots of opium, when the analyst representing one side persistently obtained higher figures than the other side. The differences were found to be due to nothing else than insufficient washing with the alcohol solution of morphine. The procedure of washing as here advocated was used in the laboratories of the late Dr. E. R. Squibb when the writer was in his employ and made many such assays.

In the B. P. it has been sought to overcome the variable error due to impurities in the morphine by an attempt to determine the actual morphine in the crude crystals by titration with acid and by adding to the quantity so found the quantity assumed to remain in the precipitate liquors. The same procedure has sometimes been proposed for use with the U. S. P. method. With lime methods this is doubtless a nearer approach to accuracy, though sources of error still remain. With the U. S. P. method this plan is liable to lead to much too high results.

Manufacturers of opium alkaloids have long known the difficulty of separating codeine from morphine by means of ordinary processes of crystallization and precipitation, and morphine compounds

of the market commonly contain this alkaloid; up to a few years ago it was not unusual to find 5 per cent. or more. But the fact that morphine separated from opium under the conditions of the assay methods now under discussion may contain up to 3 per cent. of its weight of ether- and chlorform-soluble alkaloid, chiefly codeine, seems to have escaped general notice, so far as the literature on opium assay is evidence. Codeine, being a strong base, is consequently included as morphine in titrations of the crude alkaloid. Even after a second precipitation from a lime solution containing alcohol, in the "Mallinckrodt Re-assay," the writer has invariably found in morphine from all types of precipitation processes from 1 to 2 per cent. of codeine, whenever he has looked for it. In view of the ready solubility of free codeine in all of the liquids used in both of the processes being discussed, this might well be doubted by those who have not proved it for themselves. That is easily done, however, by dissolving the twice-precipitated morphine in fixed alkali solution and shaking out with ether. The residue remaining after evaporation of the ether will usually yield the codeine pure enough for identification by means of the customary color reactions and the melting-point.

In the morphine from the comparative assays by the B. P. method, reported above, other alkaloids were found equivalent to 2.31 per cent. of its weight of codeine, as determined by titration of the extract obtained with immiscible solvent; in that from each of two pairs of assays by the U. S. P. method, 2.21 and 2.34 per cent., respectively, were found. It will be seen that the discrepancy caused by including this in the titration as morphine cannot be ignored when the highest possible degree of accuracy is desired.

Another source of variable error, also additive in its effect, is often overlooked by those advocating titration of morphine obtained by either of the two types of methods. Lime methods cause contamination of morphine with varying quantities of matter insoluble in both alcohol and lime water, and these often neutralize enough acid to introduce an appreciable error in the titration. The alkalinity of these substances is, at least in part, due to presence of calcium carbonate, which cannot be entirely excluded because of the nature of the method. Morphine from U. S. P. assays sometimes contains more than 10 per cent. of its weight of matter insoluble in alcohol or lime water, of which calcium ammonium meconate forms a large proportion. It is well known that this insoluble matter may neutral-

ize much mineral acid under the ordinary conditions of alkaloid titration. If, therefore, the B. P. procedure of titrating the crude morphine be applied to the U. S. P. method, the final results will in many cases be very much too high.

An example will illustrate the effect of only a small quantity of such insoluble impurities, also that of an average amount of chloroform-soluble alkaloid.

The sample of opium reported upon above yielded in one case 12.49 per cent. of crude morphine by the U. S. P. method. The lime-water correction applied to a portion of this gave 12.21 per cent. as the final result by that method. Another portion was dissolved in N/10 acid and titrated back with N/20 alkali, with methyl red as indicator. Another portion was boiled with alcohol and the insoluble matter filtered out and washed until the washings were free from alkaloid. This insoluble matter was also titrated. The alcohol solution and washings were evaporated to dryness, the residue dissolved in caustic soda solution and shaken out with chloroform. The filtered chloroform solutions were evaporated to dryness and the residue titrated. The results were as follows:

| | | N/10 acid required |
|---|---|---|
| 1.249 Gm. of crude morphine | | 40.39 Cc. |
| Alcohol insoluble matter in it | 1.11 Cc. | |
| Chloroform soluble matter in it | 0.87 Cc. | |
| | | 1.98 Cc. |
| Actual morphine in it (so far as known) | | 38.41 Cc. |
| 38.4 Cc. of N/10 acid represent | 1.156 Gm. of morphine | |
| Additive correction for solubility of morphine in precipitate liquors | 0.056 Gm. | |
| | 1.212 Gm., or 12.12 per cent. of morphine. | |

Had the correction for other alkaline substances in the crude morphine been omitted, the result by titration would have been 12.72 per cent., obviously too high. That the U. S. P. (Squibb) method may give results that agree closely with those arrived at with this more complicated procedure is also shown by this example, but data are at hand indicating that this may be rather an exception. Two samples of "gum" opium (sources unknown) gave distinctly higher

results by the official method, and in triplicate tests of one of them there was also a greater variation in the result than when corrections for impurities and solubility were made. These differences are shown below.

| | Per cent. morphine | |
|---|---|---|
| Opium | U. S. P. method | U. S. P. method corrected |
| (1) | 11.40 | 11.01 |
| (2) | 14.91 | 14.44 |
| | 14.68 | 14.35 |
| | 14.79 | 14.37 |

It is difficult to escape the conclusion that the U. S. P. method with lime-water correction only has a tendency of giving somewhat too high figures.

The solubility figure used above was determined as follows: One gramme of fully hydrated morphine, free from uncombined moisture and chloroform-soluble alkaloids, was dissolved in a moderate excess of dilute sulphuric acid. The solution was diluted with water to 20 Gm., then subjected to the U. S. P. procedure for precipitation of morphine. After standing over night at room temperature (during hot weather) the mixture was kept at 15° to 16° for three hours, the morphine then filtered out, washed and dried as usual. The loss, which scarcely differed in duplicate determinations, was 0.056 Gm.

It is not a simple matter to determine accurately the small quantity of morphine remaining in assay liquors, which is mixed with a much larger quantity of other alkaloids and other interfering materials. The few attempts so far made by the writer, as time permitted, by means of ether, iso-butyl alcohol and chloroform mixture, etc., gave results far from convincing, and for that reason these are not included in this report. The figure obtained with pure morphine is probably only slightly lower than the quantity of morphine lost in actual assays, provided the necessary conditions for obtaining a maximum precipitation are strictly adhered to, particularly in regard to sufficient agitation, time allowance, and low temperature. Moreover, it is quite possible that any small deficiency in this solubility figure may be counterbalanced by small quantities of alkaline impurities in the morphine that have not been discovered and, therefore, are not allowed for.

The B. P. assays given in this paper were also checked by a correction for alkalinity of substances soluble in chloroform and insoluble

in alcohol. In comparison with the same procedure applied to the U. S. P. assays of the same sample the following differences are shown:

| | U.S.P. | B.P. |
|---|---|---|
| Official method ..... | 12.21 per cent. | 12.38 per cent. |
| Corrected ..... | 12.12 per cent. | 11.96 per cent. |

Although corroboration of the data presented in this paper by comparative tests of all kinds of opium are very desirable, there is enough evidence to warrant at least the tentative inference that both the U. S. P. and the B. P. method have a tendency toward somewhat too high results, but that neither method is liable to give results very far from the truth.

For rapid approximate results the writer favors lime methods and methods of the type adopted by the German Pharmacopœia of 1910, as they are expeditious and require comparatively little labor, but for the highest degree of precision possible under the present conditions of incomplete knowledge he would recommend the Squibb method as given in full detail in Ephemeris, vol. 3, p. 1150, and in the United States Dispensatory, nineteenth edition, with omission of the lime-water correction and substitution for it of titration of the morphine, corrections to be made for alkaline impurities and for solubility. Several variations in procedure being possible, the following is proposed as the simplest:

### Correction for U. S. P. (Squibb) Method of Opium Assay.

Mix thoroughly the weighed crude morphine from 10 Gm. of opium and divide it in two equal portions. Boil one portion in a 100-Cc. flask with about 50Cc. of neutral (preferably absolute) alcohol, reserving the other for a duplicate determination or for use in case of accident. Continue heating until there is no further visible diminution of undissolved residue. Filter out insoluble matter and wash it with hot alcohol until the washings are free from alkaloid. Dilute the filtrate and washings with an equal volume of distilled water that has been rendered neutral to methyl red, if necessary, and titrate the solution with N/10 acid, using methyl red as indicator. Evaporate the alcohol from the titrated solution below a boiling temperature, add fixed caustic alkali solution moderately in excess of the quantity required to convert the morphine into alkali morphinate, and shake it out with three 10-Cc. portions of chloroform. Filter

the chloroform extracts successively through a small, dry filter, wash the filter with chloroform, and evaporate filtrate and washings to dryness. Determine the volume of N/10 acid required to neutralize the extracted matter and subtract it from the volume required for the first titration. The remainder, multiplied by 2, gives the volume of N/10 acid representing the morphine in the crude alkaloid from 10 Gm. of opium. To the weight of hydrated morphine so found add 0.056 Gm. The sum, multiplied by 10, gives the percentage of hydrated morphine in the opium.

The volumetric solutions should be standardized with pure morphine and the titrations for that purpose performed in the same way as in actual determinations.

The procedure advocated above is applicable also to lime and other precipitation methods, with a suitable readjustment of the solubility figure.

The writer agrees with Dr. Dohme [2] that shaking-out methods are likely in the future to supplant precipitation methods of opium assay, but he also concurs in the view of Dr. A. B. Lyons [3] that these newer methods still require a thorough trying-out to establish their reliability and their superiority over those generally accepted. In trial of published shaking-out methods one is struck with the great tedium attending complete removal of other alkaloids before shaking out the morphine, and the difficulty of obtaining a precise end-point in titrations because of the presence of much color and substances that not only obscure the color changes of indicators, but also impair their sensitiveness. If authors of such processes would publish them in complete detail, it is possible that others might be able to obtain with them such satisfactory results as they do. As it is, each person trying them must waste considerable time in working out the details himself.

## Summary.

The conclusion, which requires confirmation with opium of abnormal composition, has been reached that the U. S. P. and B. P. methods give fairly accurate results, with a tendency toward somewhat too high results.

---

[2] *Loc. cit.*

[3] *Ibid.*, p. 97.

A method of double titration is proposed, by means of which a nearer approach to accuracy may be attained through elimination of sources of variable error due to presence of alkaline substances other than morphine in the crude morphine obtained in precipitation methods.

A solubility correction figure has been determined for the U. S. P. (Squibb) method and is proposed for use in conjunction with the double titration.

Carl E. Smith Testing and Research Laboratory,
5 Beekman Street, New York.

## NOTE ON ALGERITA ROOT.[1]

By MERRILL C. HART.

The supposed therapeutic properties of algerita root had been suggested to us as a subject worthy of a more extended investigation, particularly because it was stated that there was a possibility of the presence of hydrastine. This plant comes into pharmaceutical notice because of its use by Mexicans and old settlers in western Texas. Infusions of the root are used for "eye sores," while chewing the roots is considered reliable as a corrective for "sore mouths." Injections of an infusion have been used for gonorrhœa. Although the appearance of the root, as well as its botanical relationships, indicated that it differed but slightly from common barberry as to its alkaloidal constituents, a brief study was carried out.

The material examined consisted of the roots of *Odostemon trifolatus* (Moric.) Heller[2] (*Berberis trifoliatus,* Moricand), a member of the Berberidaceæ. Algerita grows most abundantly in the rough country and along the foot-hills of western Texas and New Mexico, and extends down into adjacent Mexico. It is a rigid shrub,[3] 2.5 to 30 dm. tall; leaflets rigid and coriaceous sessile on the apex of the petiole, oblong or lanceolate, 3 to 7 lobed or toothed, the teeth and tip spinescent; flowers, saffron-scented; berries, globose, and the size of a pea.

[1] Contribution from the Chemical Research Laboratory, the Upjohn Company.

[2] Muhlenbergia 7, 139, 1912.

[3] Robinson, B. L., "Synoptical Flora of North America."

A quantity (210 g.) of the finely ground root was exhausted by percolation with hot 95 per cent. alcohol. The percolate was concentrated to a volume of 450 Cc., and then 150 Cc. ether and 15 Cc. of sulphuric acid were added. A yellow crystalline deposit of berberine sulphate separated, and this was filtered off on suction after several days. Various procedures failed to increase the yield above that obtained in this manner. The weight of berberine sulphate was 3.38 g., equivalent to 1.31 per cent. berberine. After one crystallization from dilute alcohol containing sulphuric acid it was analyzed.

0.3983 g. gave 0.2179 g. $BaSO_4$.

Calc. for $C_{20}H_{17}NO_4.H_2SO_4$ : $H_2SO_4 = 22.6$; found 22.9 per cent.

The berberine sulphate, when treated with a solution of sodium hydroxide, turned dark red at first, and upon further addition of alkali a citron yellow precipitate of berberinal was formed. It melted at 143° to 144°.

The original filtrate from the berberine sulphate was diluted with water and concentrated somewhat to remove the ether and some of the alcohol. It was then rendered alkaline and repeatedly extracted with ether. The solvent was removed and the residue (1.3 g.) was dissolved in alcohol and put aside. After prolonged standing considerable non-alkaloidal material separated. The entire fraction was taken up in 5 per cent. sulphuric acid. The acid solution was exhaustively extracted with ether and with chloroform, and then rendered alkaline with ammonia. The alkaloidal material now extracted with ether and with chloroform weighed 0.25 g. (0.11 per cent.).

The original filtrate from the berberine sulphate which had been extracted with ether was repeatedly extracted with chloroform (2.5 L.). After removing the solvent, the residue yielded a further quantity of berberine as sulphate, amounting to 0.465 g. of berberine sulphate. This brings the yield of berberine up to 1.49 per cent. This fraction contained also a slight amount of syrup of alkaloidal nature, from which nothing of a crystalline nature was obtained.

The original solution was now practically free from alkaloid. It is thus shown that the alkaloidal material present in Algerita root is essentially berberine. The amount of berberine in *Berberis vulgaris* is about 1.3 per cent., while Algerita yielded 1.49 per cent. Hydrastine is absent in Algerita, and the associated alkaloids are present in quantities amounting to approximately 0.1 per cent.

Kalamazoo, Michigan, April 10, 1916.

# THE ASSAY OF SPIRIT OF PEPPERMINT.

By H. L. THOMPSON, College of Pharmacy, University of Nebraska, Lincoln.

An article entitled " Estimation of Oil of Peppermint in Spirit of Peppermint," by Chas. H. LaWall, appeared in the December, 1913, issue of the *Journal of the American Pharmaceutical Association.* This method was tried out, and is good in calculating percentage by volume of alcohol and of oil of peppermint. The one objection to this method is that the addition of the hydrochloric acid destroys the menthyl acetate content of the oil of peppermint used in making the spirit of peppermint, and the possibility of a true analysis of the original oil is thereby lost. Furthermore, the amount of spirit used allows an insufficient amount of oil to be used in further assay.

Many oils of peppermint have appeared on the market which are not rectified, and which, in many cases, are dementholated or adulterated. These oils, being much cheaper, are often used in making the spirit of peppermint. It is therefore necessary not only to determine the amount of oil in the spirit, but the quality of the oil used, and it was with this idea in view that this work was undertaken.

There are seventeen substances in oil of peppermint, and, according to Power and Kleber, in the assay, all the esters are calculated as menthyl acetate, and the alcohols as menthol. The menthone content is usually neglected.

Into a tared 50 c.c. volumetric flask, at 20° C., introduce 50 c.c. of spirit of peppermint, and note the weight of the spirit.

Pour the spirit of peppermint into a cassia flask, and rinse the volumetric flask with three 10-c.c. portions of distilled water at about 50° C., and add to the cassia flask. Then rotate the flask, and add sufficient water to bring the oil into the neck of the cassia flask; stopper, and let it stand for four or more hours.

Then read the volume of the oil and calculate the percentage by volume of oil in the spirit by dividing the volume of the oil by the volume of the spirit, and multiplying by 100 to give direct percentage.

Separate as much of the oil as possible by means of a small pipette, using a 1- or 2-c.c. pipette, or a dropper, being careful not to draw out any of the aqueous layer, and filter the oil into a previously-weighed graduated cylinder of 10 c.c. capacity, graduated to tenths of a cubic centimetre. Weigh the cylinder and oil, noting volume and weight of the oil.

Calculate the weight of the oil in the spirit of peppermint from the number of cubic centimetres in 50 c.c. of the spirit compared to the volume and weight of the filtered oil in the 10 c.c. graduated cylinder, by ratio and proportion; namely, c.c. of oil in 10 c.c. cylinder: weight of oil in 10 c.c. cylinder : : c.c. of oil in spirit : $x$, or the weight of oil in spirit.

Use the weight obtained as the weight of the oil in 50 c.c. of spirit in calculating for menthyl acetate and menthol.

Separate the few drops of oil remaining by means of a filter-paper in rolls, introduced into the neck of the cassia flask to absorb the excess oil. Keep the hydro-alcoholic liquid to determine the percentage of alcohol by weight and volume.

Pour the filtered oil of peppermint into an Erlenmeyer flask and note its weight by difference. To this add 25 c.c. half-normal alcoholic sodium hydroxide, and boil on a water-bath with a reflux condenser for one hour. Add 3 drops of phenolphthalein indicator, and, if the red color is very difficult to see, dilute with 50 to 100 c.c. of distilled water. Titrate back the excess of half-normal alcoholic sodium hydroxide with half-normal hydrochloric acid.

Note the number of cubic centimetres of half-normal alcoholic sodium hydroxide consumed, and calculate the percentage of menthyl acetate as per tables appended.

Transfer the solution to a Squibb's separatory funnel, and wash the residual oil, which contains menthol, at least two or three times, and separate.

Transfer the oil to an acetylization flask, add 1 gramme of anhydrous sodium acetate and 5 c.c. of acetic anhydride, and boil gently for one hour, using a sand-bath.

Transfer the acetylized oil to the separator, and wash twice with water, add 3 drops of phenolphthalein indicator, about 50 c.c. of water, and just enough dilute sodium hydroxide solution, preferably half-normal sodium hydroxide solution, to turn the aqueous layer pink. Wash the oil once more, and separate.

Then filter the separated oil into a 10-c.c. graduated cylinder, previously weighed. Note the volume of oil and weight of cylinder and oil. Pour the acetylized oil into another Erlenmeyer flask, and note its weight by difference. Add 25 c.c. half-normal alcoholic sodium hydroxide, and boil on the water-bath with a reflux condenser for one hour. Cool, add 3 drops of phenolphthalein indicator. If the end-point cannot be clearly seen, dilute with 50 to 100 c.c. of

distilled water, and titrate back with half-normal hydrochloric acid. Note the number of cubic centimetres of half-normal alcoholic sodium hydroxide consumed. Calculate the percentage of menthol (free and as ester) by use of the appended tables.

To determine the alcohol content in the spirit, pour the hydro-alcoholic solution into a distilling flask. Rinse the cassia flask with 100 c.c. of distilled water, and add it to the distilling flask.

Distil the alcohol, collecting it in a tared 100-c.c. volumetric flask until nearly 100 c.c. of distillate are obtained. Make to volume, weigh, and determine the specific gravity. Make correction to correspond to specific gravity at 15.6° C. Obtain the percentage of alcohol by weight corresponding to the specific gravity from the U. S. P. VIII alcohol tables, pages 603 to 607, or Table II, page 203, Bulletin No. 107 (revised), Bureau of Chemistry, U. S. A. Multiply this figure by the weight of the distillate and divide by the weight of the sample of spirit of peppermint taken to obtain the percentage by weight of alcohol.

From the specific gravity of the distillate obtained under the determination by weight find the percentage of alcohol by volume from the U. S. P. VIII (revised) alcohol tables, pages 603 to 607, or from Table II, p. 203, U. S. Bulletin No. 107. Multiply this figure by the volume of distillate (calculated from the specific gravity) and divide by the volume of the sample of the spirit of peppermint, thus obtaining the percentage of alcohol by volume in the original sample of spirit of peppermint.

The appended table is based on sodium hydroxide, NaOH – 40; menthyl acetate, $C_{10}H_{19}.C_2H_3O_2$ – 198; menthol, $C_{10}H_{19}OH$ – 156,: and each twentieth of a cubic centimetre of half-normal alcoholic sodium hydroxide is equivalent to one milligramme of sodium hydroxide, which I have designated sodium hydroxide number, or NaOH No.

In calculating the percentage of menthyl acetate in the original oil, note the number of cubic centimetres of half-normal sodium hydroxide alcoholic consumed, and find its equivalent, in grammes of menthyl acetate, in the acetate column. Divide this number by the weight of the oil taken, and multiply by 100 to give the percentage. Or find the equivalent in milligrammes of sodium hydroxide, in the NaOH No. column, and divide this equivalent by the weight of the oil taken. This gives the sodium hydroxide number for one gramme of the oil. Find this number in the NaOH column, and

under the acetate column is its equivalent in grammes. Multiply that number by 100, and it reads percentage directly of menthyl acetate in the original oil.

To calculate the percentage of menthyl acetate in the spirit of peppermint, multiply the weight of the oil in the 50 c.c. of spirit by the percentage of menthyl acetate in the original oil, and divide by the weight of the 50 c.c. of spirit of peppermint. Multiply this number by 100 to obtain the percentage by weight of menthyl acetate in the spirit.

In calculating the percentage of menthol in the original oil, note the number of cubic centimetres of half-normal alcoholic sodium hydroxide consumed, and find its equivalent in grammes of menthol in the alcohol column. Divide this number by the weight of the oil minus the equivalent in the difference column, and multiply by 100 to obtain percentage. Or find the sodium hydroxide number equivalent to the cubic centimetres of alcoholic sodium hydroxide used, and divide this by the weight of the oil taken. This gives the sodium hydroxide number for one gramme of oil. Find this number, and in the alcohol in the original oil column is given the grammes of menthol in the original oil. Multiply this by 100 to read percentage directly.

To calculate the percentage of menthol (free and as ester) in the spirit, multiply the weight of the oil in the 50 c.c. of spirit of peppermint by the percentage of menthol in the original oil and divide by the weight of the 50 c.c. of spirit of peppermint. Multiply this by 100 to obtain the percentage of menthol (free and as ester) in the spirit of peppermint.

Or use the following formulas:

For menthyl acetate in oil:

$$\frac{\text{c.c. N/2 sol.} \times 9.9}{\text{Weight of oil taken}} = \text{per cent. of menthyl acetate in oil.}$$

For menthyl acetate in spirit:

$$\frac{\text{Weight of oil} \times \text{per cent. acetate} \times 100}{\text{Weight of spirit}} = \text{per cent. of menthyl acetate in spirit.}$$

For total menthol (free and as ester) in oil:

$$\frac{\text{c.c. N/2 sol.} \times 7.8}{\text{Weight of oil taken}} = \text{per cent. of menthol (free and as ester) in oil.}$$

For total menthol (free and as ester) in spirit:

$$\frac{\text{Weight of oil} \times \text{per cent. menthol} \times 100}{\text{Weight of spirit.}} = \text{per cent. of menthol (free and as ester) in spirit.}$$

## RESULTS.

| No. | Alcohol in spirit, Per cent. weight | Alcohol in spirit, Per cent. volume | Oil in spirit, Per cent. volume | Oil in spirit, Per cent. weight | Menthyl acetate In oil, Per cent. weight | Menthyl acetate In spirit, Per cent. weight | Menthol in Oil, Per cent. weight | Menthol in Spirit. Per cent. weight |
|---|---|---|---|---|---|---|---|---|
| A | 73.36 | 75.98 | 10.00 | 10.83 | 11.04 | 1.19 | 63.06 | 6.83 |
| B | 73.48 | 75.09 | 10.00 | 11.06 | 10.92 | 1.20 | 62.52 | 6.92 |
| C | 73.81 | 76.44 | 10.20 | 10.64 | 10.85 | 1.18 | 63.93 | 6.80 |
| D | 73.72 | 76.39 | 10.40 | 11.37 | 11.66 | 1.21 | 63.45 | 6.91 |
| E | 74.58 | 77.23 | 10.00 | 10.98 | 14.08 | 1.54 | 62.62 | 6.87 |
| F | 78.96 | 81.78 | 10.00 | 11.10 | 12.76 | 1.42 | 63.43 | 6.88 |
| G | 74.03 | 76.33 | 10.00 | 11.05 | 13.69 | 1.52 | 59.86 | 6.61 |
| H | 79.08 | 81.87 | 10.40 | 11.01 | 10.65 | 1.17 | 63.15 | 6.95 |

## TABLES.

| Na No. | N/2 Al., NaOH c.c | Acetate | Alcohol | Alcohol in original oil | Difference |
|---|---|---|---|---|---|
| 1 | 0.05 | 0.00495 | 0.0039 | 0.00390 | 0.00105 |
| 2 | 0.10 | 0.00990 | 0.0078 | 0.00782 | 0.00210 |
| 3 | 0.15 | 0.01485 | 0.0117 | 0.01246 | 0.00315 |
| 4 | 0.20 | 0.01980 | 0.0156 | 0.01565 | 0.00420 |
| 5 | 0.25 | 0.02475 | 0.0195 | 0.01960 | 0.00525 |
| 6 | 0.30 | 0.02970 | 0.0234 | 0.02355 | 0.00630 |
| 7 | 0.35 | 0.03465 | 0.0273 | 0.02750 | 0.00735 |
| 8 | 0.40 | 0.03960 | 0.0312 | 0.03146 | 0.00840 |
| 9 | 0.45 | 0.04455 | 0.0351 | 0.03543 | 0.00945 |
| 10 | 0.50 | 0.04950 | 0.0390 | 0.03941 | 0.01050 |
| 11 | 0.55 | 0.05445 | 0.0429 | 0.04340 | 0.01155 |
| 12 | 0.60 | 0.05940 | 0.0468 | 0.04750 | 0.01260 |
| 13 | 0.65 | 0.06435 | 0.0507 | 0.05140 | 0.01365 |
| 14 | 0.70 | 0.06930 | 0.0546 | 0.05541 | 0.01470 |
| 15 | 0.75 | 0.07425 | 0.0585 | 0.05943 | 0.01575 |
| 16 | 0.80 | 0.07920 | 0.0624 | 0.06346 | 0.01680 |
| 17 | 0.85 | 0.08415 | 0.0663 | 0.06750 | 0.01785 |
| 18 | 0.90 | 0.08910 | 0.0702 | 0.07155 | 0.01890 |
| 19 | 0.95 | 0.09405 | 0.0741 | 0.07543 | 0.01995 |
| 20 | 1.00 | 0.09900 | 0.0780 | 0.07786 | 0.02100 |
| 21 | 1.05 | 0.10395 | 0.0819 | 0.08374 | 0.02205 |
| 22 | 1.10 | 0.10890 | 0.0858 | 0.08783 | 0.02310 |
| 23 | 1.15 | 0.11385 | 0.0897 | 0.09192 | 0.02415 |
| 24 | 1.20 | 0.11880 | 0.0936 | 0.09602 | 0.02520 |
| 25 | 1.25 | 0.12375 | 0.0975 | 0.10013 | 0.02625 |
| 26 | 1.30 | 0.12870 | 0.1014 | 0.10424 | 0.02730 |
| 27 | 1.35 | 0.13365 | 0.1053 | 0.10862 | 0.02835 |
| 28 | 1.40 | 0.13860 | 0.1092 | 0.11239 | 0.02940 |
| 29 | 1.45 | 0.14355 | 0.1121 | 0.11562 | 0.03045 |
| 30 | 1.50 | 0.14850 | 0.1160 | 0.12011 | 0.03150 |
| 31 | 1.55 | 0.15345 | 0.1209 | 0.12497 | 0.03255 |
| 32 | 1.60 | 0.15840 | 0.1248 | 0.12915 | 0.03360 |

| Na No. | N/a NaOH Al., c.c | Acetate | Alcohol | Alcohol in original oil | Difference |
|---|---|---|---|---|---|
| 33 | 1.65 | 0.16335 | 0.1287 | 0.13332 | 0.03465 |
| 34 | 1.70 | 0.16830 | 0.1326 | 0.13750 | 0.03570 |
| 35 | 1.75 | 0.17325 | 0.1365 | 0.14170 | 0.03675 |
| 36 | 1.80 | 0.17820 | 0.1404 | 0.14598 | 0.03780 |
| 37 | 1.85 | 0.18315 | 0.1443 | 0.14672 | 0.03885 |
| 38 | 1.90 | 0.18810 | 0.1482 | 0.15436 | 0.03990 |
| 39 | 1.95 | 0.19305 | 0.1521 | 0.15896 | 0.04095 |
| 40 | 2.00 | 0.19800 | 0.1560 | 0.16384 | 0.04200 |

## GERMAN DRUG PRICES FOR 1916.

By BERTHA MUELLER, P.D., Assistant Pharmacist of the German Hospital, Philadelphia.

The official edition of the "Deutsche Arzneitaxe 1916" is very interesting and instructive, in as far as it shows how existing conditions are really carefully studied, and how laws are passed to meet these conditions.

The book is divided into two main parts:

I. A general discussion of the methods for determining the price of a compound medicine and,

II. A price list of the more frequently used drugs and medicines.

In Germany the price of a compound medicine is to be determined:

1. By the price of the ingredients that enter into its manufacture.

2. By the permissible price for time and labor required in preparing and dispensing the same.

3. By the permissible charge of the container in which the medicine is dispensed.

The selling price of drugs and preparations must be based on the purchase price of the crude drug according to specified rules. This constitutes the foundation price. If a drug must be comminuted, a certain specified sum is permitted to be charged. This sum varies with the time and labor required for preparing powders of different degrees of fineness. Provisions are also made for charging a specified sum for packing and freight.

The price of a galenical is calculated from:

1. The price of the individual drug quantities that enter into its manufacture.

2. The charges permitted for time and labor.

3. The permissible compensation for loss of material during manufacture in cases where such loss is sustained.

In order to compensate for the average loss (which amounts to about 10 per cent.) sustained in the manufacture of galenicals, the selling price of such galenicals, calculated from the price of the crude drugs that enter into their manufacture plus the permissible charges for time and labor, is raised by one-ninth its value. A table is included giving the charges that may be made for time and labor required in preparing the various galenicals. The price is fixed for one kilogram quantities.

The permissible charges for compounding and dispensing a medicine are given in considerable detail. A table is included giving fixed prices for preparing definite quantities of solutions, decoctions, infusions, ointments, pastilles, pills, suppositories, etc. The apothecary, in compounding and dispensing a medicine, must calculate charges for work done according to this standard.

The charges for containers are also a matter of detailed consideration, and a price list is appended for the various containers. For clean containers returned to pharmacies for renewal, full credit must be allowed.

The following rules exist concerning the use of containers in dispensing medicines to public institutions and charitable organizations, and in dispensing medicines for veterinary purposes:

If medicines are dispensed to public institutions and charitable organizations, and for veterinary purposes, the more expensive containers, as glass-stoppered bottles, white porcelain ointment jars, pasteboard boxes, etc., may only be charged for if the prescriber has ordered the medicine to be dispensed in such a container. If, however, powders or pastilles containing opium, or any of its alkaloids, or chloral hydrate are dispensed, they must be put into a pasteboard box, and permission is given to charge for the container. In dispensing eye-salves, it is permitted to use white porcelain jars with lids and charge for them.

The price of a prescription is computed from the official price lists, and it is required that the individual parts that compose the selling price be recorded in detail on the prescription. If any prescription is of such a nature that an ingredient (an excipient, for instance) which the prescriber failed to write for must be added, and such ingredient influences the price of the finished preparation, the apothecary must make a record of the same on the prescription. An extra charge is permitted for all prescriptions filled during the hours from 9 P.M. to 7 A.M. (night price).

The selling price of all medicines sold in original containers is based on their purchase price according to specific rules. Charges for dispensing may not be made if the preparation is sold in original container. If, however, a smaller quantity is ordered than the original package contains, the apothecary doubles the purchase price and charges for dispensing and for the container.

Homeopathic tinctures and dilutions thereof come under a separate price list. All charges for work done in preparing and dispensing such medicines are calculated according to the official Time and Labor Compensation price list.

Charges for special messenger, postage, etc., can be made only if the dispenser can prove that he has incurred and has notified the purchaser in advance of such extra expenses.

Drugs that are protected by patent or by trade-mark patents are enumerated in the price list, both under the protected and under the free or scientific name, and the price to be charged for the medicine as dispensed is to be determined by the name under which the drug was ordered.

To the American pharmacist the book is of interest primarily as an illustration of the comprehensive and thorough system prevailing in Germany at the present time to safeguard all parties interested

By this system the public, especially, is protected against overcharges and a uniformity of prices of widely-used commodities is secured.

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## GENERAL PROBLEMS AND TENDENCIES IN CANCER RESEARCH.[1]

By Prof. Leo Loeb.[2]

After the successful continuous transplantation of rat sarcoma and mouse carcinoma had shown that we possessed a method suitable for the study of the biology of tumors, and which promised a rich harvest of results, the decade following the year 1901 was to a great extent devoted to the study of propagated tumors rather than to the analysis of the first origin of tumors, although this latter problem had never been entirely neglected. Within recent years, however,

[1] An address before Section VIII of the II Pan-American Scientific Congress on January 5, 1916.

[2] Reprinted from *Science*, N. S., vol. xliii, No. 1105, pp. 293–303, March 3, 1916.

much attention has been given to the origin of tumors. The so-called endemic occurrence of cancer which we observed in the case of cattle and rats, and which certain investigators noted in the case of mice and other animals, suggested to us sixteen years ago the possible significance of heredity as an etiological factor. Some years later, observations which we made in a mouse-breeding establishment in Granby confirmed this hypothesis; but it is only during the last six years, following the observations of Tyzzer and Murray, that our investigations, carried out in conjunction with Miss Lathrop, proved on a very broad basis the very great significance of heredity in the transmission of cancer in mice, the partial independence of the age and frequency factors, and the correlation between cancer frequency and structural and functional characteristics of the animal. The results of hybridization experiments which we carried out on a large scale indicate that in some crosses the tendency to a high cancer rate may be dominant, while in some others the opposite tendency predominates, and in a few an intermediate result is obtained. Our experiments established for the first time the cancer rate for a number of different strains; each strain was followed through several successive generations and in each generation a large number of animals were observed. The resultant figures for the various generations of the same strain were usually in fairly close agreement. Animals belonging to such strains were used for hybridization experiments. The results of hybridization experiments which we obtained do not seem to be compatible with the view recently expressed that the tendency to cancer is of a recessive character and that all results can be explained on such a basis.[3]

Of a different character is a problem in heredity first studied by E. E. Tyzzer. It is well known that some strains of mice are a favorable soil for a certain transplantable tumor, while other strains are not. In crossing a favorable and an unfavorable strain Tyzzer found conditions apparently incompatible with Mendelian principles. We obtained likewise, in subsequent experiments with M. S. Fleisher, results similar to those of Tyzzer, and we suggested that the results might be explained by assuming the presence of multiple factors. The same interpretation may apply to the heredity of autochthonous tumors to which we referred above and in which also simple Mendelian proportions do not seem to exist.

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[3] Maud Slye, *Interstate Medical Journal*, XXII, July, 1915, p. 692.

These studies of the cancer incidence in various strains of mice and the methods used therein have, however, a much wider significance. On the basis of a thorough knowledge of the cancer incidence in certain families, and on this basis alone, will it be possible to analyze certain other factors in the etiology of tumors, and the understanding of these latter factors, as well as of heredity, will perhaps ultimately provide us with a rational basis for the prevention of cancer. Without a thorough knowledge of heredity, conclusive results as to the significance of other factors could not be expected. Acting on this principle, we found that certain castration in sexually mature mice at the age of three to eight months reduces the cancer rate in a very pronounced way. Prevention of pregnancy, while it still has some effect in reducing the cancer rate, as we found several years ago, has very much less significance than castration.

These results and some additional ones to be mentioned shortly permit us to classify the causes of tumors into two main divisions, internal and external ones. Heredity belongs to the former class. The point of attack of these heredity factors we do not yet know. In some cases, they may perhaps stand in relation to some other internal factors, which are in all probability of significance in certain cases. I refer to the spontaneous parthenogenetic development of the egg within the ovary and elsewhere in mammals, a process which, according to our findings in the guinea pig, is not a rare occurrence, and may even normally proceed to the formation of the anlage of the central nervous system. To this class of factors may also belong developmental errors which were already suspected by Cohnheim and which as we know may appear as inheritable mutations in various groups of animals.

The external factors may be further divided into chemical and mechanical, and both may be derived either from within the body or from the outside world. As an example of a chemical factor originating within the body, we may cite the great importance of the internal secretion of the corpus luteum in the origin of cancer in mice to which we referred above, but other internal secretions will probably be found to be of similar significance. External mechanical factors can be recognized in the well-known effect of chronic irritation. How far certain parasites, especially those in the class of vermes and insects, produce cancer through chemical and how far through mechanical means is not certain. Previous observations in man in the case of cancer of the bladder caused, directly or in-

directly, by bilharzia, and especially the recent experiments of Fibiger make it, however, quite certain that such parasites may be the cause of cancer. It is likewise uncertain how far Röntgen-ray cancer, frequent in Röntgen-ray operators, and also apparently experimentally produced in a few rats by Marie, is due to ulceration subsequent to exposure to or to the direct stimulating action of the rays. In some cases perhaps chemical and mechanical factors may coöperate in producing tumors; the efficiency of such a combination in calling forth tumor-like formations has been shown by us in the case of deciduomata of the uterus, which we produced experimentally, a new formation which we included in a class designated as transitory tumors.

There are observations on hand which indicate that growth stimuli may be especially active in animals with an hereditarily determined tendency to cancer. Such an observation we made in the case of a cancer in a mouse belonging to a family rich in tumors, where ulceration of the skin near an adenoma of the mammary gland led to the development of an epidermal carcinoma. Further systematically conducted experiments in this direction might lead to interesting results.

It is, however, not probable that in order to obtain the production of cancer there must be a definite quantity of prerequisite internal factors. On the contrary, there is some evidence on hand which makes it probable that internal and external factors may vary in inverse ratio, and that if the external factors are quantitatively very strong, the quantity of internal factors may be reduced.

If we survey briefly the various types of growth reactions known in vertebrates, we may, perhaps, according to the character of the stimuli, which are usually in each case the first members in a complicated reaction chain, and according to the character of the systems on which they act, provisionally distinguish the following types:

1. Various stimuli act for a short time on complex systems, the egg-cells, and lead to a long chain of growth phenomena which ultimately cease. The experiments in artificial parthenogenesis of Jacques Loeb led to a very far-going analysis of these phenomena.

2. Defects lead to a chain of growth phenomena, which are of a temporary character, and which come to a standstill after a certain quantity and kind of new-formed tissue has more or less completely filled out the defect.

3. Chemical substances stimulate the growth of certain tissues to which they bear a more or less specific relation. These growth phenomena come to a standstill with the activity of the stimulating substance or very soon afterwards (corpus luteum and mammary gland).

4. A combination of factors 2 and 3 may lead to tumor-like growth phenomena when either factor alone would cause only a slight proliferation. Here, again, the effect is temporary (experimental deciduomata of the uterus).

5. Chemical (fat soluble?) bodies which do not show a specific relation to the organs affected stimulate various tissues to a temporary proliferation; fat soluble stains (Bernhard Fischer and others) and ether (Reinke) are substances that under certain conditions seem to exert a stimulating effect.

6. Chemical and mechanical factors produce with the aid of a large quantity of internal factors, or in certain cases apparently without such aid, an increase in cell proliferation that persists after the stimuli have ceased, which is permanent, potentially of unlimited duration in contradistinction to the temporary reactions mentioned above. This is the cancerous reaction with which all or at least the large majority of the mammalian tissues may respond. Neither potential immortality—some, or perhaps all, somatic cells are potentially immortal—nor the power of continued proliferation, which in all probability even certain ordinary somatic cells possess, is characteristic of this reaction, but rather the increase in proliferative power, and furthermore, the permanency of the reaction in response to a temporary, non-permanent stimulus. We have then to assume that a labile cell-system which responds to temporary stimuli with a temporary reaction is transformed under the influence of certain stimuli, and often with the aid of hereditary factors, into a stable system which shows a greater proliferative power than the labile system. The stimulus thus brings about merely a transformation of the cells into a new kind of cell-system, which proliferates indefinitely at a more or less increased rate. Such a transformation may be called a mutation.[4] Inasmuch as all, or the large majority of all, body cells are liable to this change, they must have

[4] We would have to deal in this case with a mutation not in a germ cell, but in a somatic cell. For a more detailed discussion of this problem *cf.* Leo Loeb, "Germ Cells and Somatic Cells," *American Naturalist*, vol. 49, 1915, p. 286.

from the beginning in their organization a mechanism that provides for the possibility of such a mutation.

According to this conception, we must then assume that all or most cells have potentially two equilibria, the normal one and the cancerous; they begin life with the normal equilibrium, but under the influence of certain stimuli, with or without the coöperation of hereditary factors, they are transferred to the cancerous equilibrium.

Cells in the normal equilibrium react to stimuli in the manner indicated above (types 1 to 5); ultimately they return invariably to the normal equilibrium after the stimulus has ceased to act. Cancerous cells, on the other hand, may perhaps be exterminated, but they are not known to return to the normal equilibrium.

There is, however, an alternative to this conception which would eliminate the necessity for assuming a new equilibrium for cancerous proliferation, an assumption for which naturally no analogy can exist. If we assume that an external agent associated with the cell, rather than a physico-chemical mechanism within the cell, produces the cancerous proliferation, the latter would no longer represent a unique condition, but would be a special application of one of the types 3 to 5, in which, however, the stimulus would act incessantly. Such a stimulus could be supplied through multiplying microörganisms which essentially represent constantly newly formed external chemical stimuli. Such microörganisms would not be identical with bacteria causing various ordinary infectious diseases. As we have shown at an early stage of our investigations, cancer among animals is not infectious in the sense in which certain other diseases are infectious. We could feed tumor tissue to normal animals or keep normal animals in the same cage with cancerous animals without a transfer of the disease taking place; neither could Ehrlich produce cancer in young mice which were suckled by cancerous animals. But this does not exclude the possibility that certain other organisms might play a certain rôle. We know that microorganisms can call forth cell multiplication in plants and animals. In plants, certain bacteria can produce, as has especially been demonstrated in the case of the crowngall by Erwin F. Smith, tumor-like proliferation—a result depending in this case not merely on the kind of stimulus, but also on the particular system on which the stimulus acts. In this connection we might also mention a number of extremely interesting cases in which various investigators saw the transformation of normal into cancerous tissues, subsequent to

contact with cancerous tissue of another kind, but in the same individual. I referred above to an observation of this character in which we found skin to become cancerous under the influence of an adenocarcinoma of the mammary gland. Similarly in contact with carcinoma, connective tissue may become sarcomatous. Such tumors we called combination contact tumors. In such a carcinosarcoma in a Japanese mouse which we studied experimentally, we found that the carcinomatous and sarcomatous components followed the same variation curve of growth energy in succeeding generations. This suggests the identity of the agent which causes the proliferation of both tissues and the dependence of the variation in growth upon the variation in the activity of the agent. The agent transferred from one tissue to another might be a chemical substance—an explanation first suggested in the case of the sarcomatous transformation of the stroma by Ehrlich and Apolant—or it might be a microörganism. Even under normal conditions there are indications which point to a chemical influence exerted by one tissue upon another. In this manner we interpreted the differences in cell activity in the connective tissue of the mucosa in certain organs near the epithelium on the one, and near the submucosa on the other hand. The different effect exerted by the tissues of different individuals upon the activity of the fibroblasts of the host also points to such a conclusion (different effects of auto- and homoiotransplantation).

The very important results of Peyton Rous are worthy of especial consideration. This investigator, working with fowls and employing methods which in the case of mammalian tumor had not led to positive results in the hands of earlier investigators, was able to separate by filtration and other means the causative agent from the sarcoma cells with which it was associated. In this case, we might have to deal either with filterable microörganisms, or again with chemical substances. If we accept the latter alternative, we would have to assume that the same substance that initiated the cancerous cell proliferation in normal cells would, after the change has once been accomplished, be perpetually newly formed within the proliferating cells. This condition would in some respects be comparable to an autokatalytic process.[5] The cancerous equilibrium

[5] Certain analogies between growth curves and autokatalytic processes have formerly been pointed out by Jacques Loeb, W. O. Ostwald, and T. B. Robertson. In the case of fowl tumors we would have in addition to deal with the new formation within the tissue cells of a substance carried to the tissues from the outside.

would represent a condition in which this growth substance is either produced in a larger quantity than it exists in normal cells, or is entirely formed *de novo.* It seems furthermore that no antibody is produced in the body-fluid against this substance. These substances do not seem to be separable from the cells in all fowl tumors, and the kinds of fowl tumors in which a separation can not be accomplished behave in this respect like the mammalian tumors. We would have to assume the existence of different substances of this kind, and different substances always call forth a specific activity of connective tissue cells resulting in the reproduction of the original kind of tumor, and stimulating endlessly the production of the same specific substance within the fibroblasts. Just as in the case of the corpus luteum substance which is responsible for the production of deciduomata, the coöperation of a mechanical factor seems to be essential for the stimulation of tumor growth in fowl. We would most probably have to give this interpretation to these phenomena if the observation of Casimir Funk, according to whom an alcoholic extract of the tumor contains the active agent, could be confirmed in a larger number of cases. If this should prove correct, we may expect to find corresponding conditions in mammalian cancer. A study of heredity in cancer of the fowl would close this chain of investigations, and with the analysis of internal and external factors in cancer already on a solid foundation, we could then conclude that the causes of cancer in their main outline have been satisfactorily analyzed. Of course underneath this first plane of causes there are connections which extend further into fields where they meet with other factors determining cell and tissue life in its dependence upon physical and chemical laws, and thus we are led into deeper planes of causation. But here the problems have become identical with those of general biology, the laws governing cell division and ameboid movements in cancer cells not differing from those of other cells.

In this connection a few words concerning the definition of cancer might not be out of place. It might indeed be assumed that a definition of cancer satisfying past and future research is one of the essential requirements for the fruitful pursuit of investigations. On the contrary, I believe that at the present stage of investigation progress may be retarded through premature rigidity in defining cancer, and especially through insisting on the proof that secondary tumors originate from transplanted cells. In the case of sarcoma of the rat and mouse, this proof has so far been supplied only in the rat

sarcoma of the thyroid found in Chicago, and is merely based on analogy in the case of the large majority of other sarcomata. Since it has now been shown that in sarcoma of fowl an agent associated with the tumor, but separable from it, may just as well give origin to new growths, we may well hesitate in excluding from consideration new formations which in all probability under certain conditions have their origin in transplanted cells, while in other cases they may perhaps be propagated through an agent associated with the tumor. I refer here especially to the so-called lympho-sarcoma or small round cell sarcoma of dogs which, after transplantation in dogs, apparently grows from the transplanted cells (Sticker, Ewing and Beebe, and L. Loeb), while in the fox, according to von Dungern, the tumor cells are composed of host tissue. May we not, in case von Dungern's view should prove correct, have to consider the possibility that the transplanted dog cells perished in the foreign species, and that the associated agent stimulated the host cells to proliferation?

With the factors which we have already analyzed—factors of heredity, of internal secretion, of external, chemical and mechanical stimulation—we are in a position to control to a great extent the cancer rate in certain species of animals. As we said, we can not yet exclude with certainty the other alternative, namely, micro-organisms, as an additional causative factor.

After so many futile attempts to establish a direct proof of their presence, further efforts of this kind do not appear promising at present. There seem, however, still other ways open through which one may approach this problem in an indirect manner.

To decide between the two alternatives which we mentioned does not only concern cancer research in the more restricted sense, but is of the greatest importance for general biology. In return for much that it received from neighboring sciences, cancer research has given something important to biology; the serial endless experimental propagation of tumors has enriched biology with a valuable instrument of research and new outlooks on the life and character of somatic cells have been gained. We may briefly mention the following facts established or very strongly suggested: In the course of our early transplantations, we found that the energy of tumor growth can be experimentally increased as well as decreased. Ehrlich explained the increase as due to a selection of rapidly growing tumors; we, however, believed from the beginning that it was

partly produced by a mechanical stimulation of the tumor cells and in addition was possibly due to chemical stimulation caused by the transfer into a new host with a different constitution of the body-fluids; in some cases perhaps processes of immunity may also enter into this phenomenon.

In conjunction with M. S. Fleisher, we noted that chemical bodies which inhibit tissue growth at a certain period in the life of tumors do not have this power at other periods. Especially are they powerless in the case of very young tumors, an observation confirmed by Keysser. But we found that such early injections produce an immunization against the later action of these substances. The proof thus given that an immunization takes place against substances (and apparently also against physical agencies) inhibiting tumor growth is, as we pointed out on previous occasions, of great importance in our attempts to arrive at a rational treatment of cancer. Our experiments suggest, furthermore, very strongly that this immunity is of a twofold character, that it originates in the host as well as in the tumor cells themselves; that this cell immunity can be transferred to a certain number of later cell generations and is to some extent specific for the substance which had called it forth. While our results, based on the observation of a very large number of animals, strongly suggest these latter conclusions, we nevertheless think it desirable to add new evidence in order to guard against a complication with variable factors.

Are we in all these cases dealing with indirect actions on the cells and with direct actions on accompanying microörganisms, or with direct actions on the cells? We rather incline to the latter view and we would suggest that an increase in chemical activity in the tumor cells—an increase perhaps restricted to certain activities—renders the latter a much finer balance in their response to certain environmental conditions through variations in growth energy than are the normal tissue cells.

As we pointed out in 1901 on the basis of Moreau's and our own experiments, cancer cells are potentially immortal in the same sense in which protozoa and germ cells are potentially immortal. All, or at least the large majority of all, normal tissue cells are potentially cancer cells, and we may therefore with full justification conclude that ordinary somatic cells are likewise potentially immortal. Like the majority of tumors, they can not be indefinitely propagated in other individuals of the same species because of the injurious action

of what we may term homoiotoxins. On the other hand, thanks to their increased growth energy and perhaps a lessened sensitiveness to homoiotoxins, the cells of certain tumors can overcome the injurious conditions existing in other individuals of the same species and be propagated indefinitely. Tumor cells and ordinary tissue cells do not differ in potential immortality (as Bashford and others assumed), but in the intensity with which they proliferate and in their destructive power.

Of equally great biological interest are the defensive reactions called forth in the host through the growth of the tumor cells. As one of the most important results, we may here state that no immunity seems to be produced through tumor growth in the animals in which the tumor originated. We found that in the case of rat and dog tumors, cells remained alive and grew after transplantation into the animal in which they originated, while they died in other individuals of the same species. Tyzzer found the same to be true in the chicken, and Haaland and Fleisher and ourselves in the mouse. Haaland's experiments suggested, furthermore, that the autochthonous tumor could not act as antigen and by proving in addition that this tumor does not neutralize immune substances, our experiments prove the correctness of Haaland's suggestion that against an autochthonous tumor no immunity can be produced. The greater significance again attached to the study of animals in which tumors originated in contradistinction to bearers of experimental tumors, is one of the characteristic tendencies of recent cancer investigation, and it is of interest in this connection to note that our experiments indicate that animals with autochthonous tumors are a better soil for the growth of other spontaneous tumors than normal animals.

While, therefore, in the organism in which the tumor originated usually no reaction takes place against tumor cells, reactions do take place after transplantation of tumor cells into other individuals. These reactions are essentially of a similar character in the case of tumors and of normal tissues. Again correlation between the behavior of normal and of cancerous tissues has proven fruitful of results in this case. After autotransplantation of a piece of normal tissue it may, in the same way as a piece of tumor, at least in the case of certain tissues, apparently live indefinitely, while after homoiotransplantation, as we observed, the tissues die as a result of the attack by lymphocytes and through the influence of fibro-

blasts of the host which produce dense fibrous tissue which in turn strangulates the foreign cells. There is a possibility that the strange body fluids may also directly interfere with the metabolism of certain transplanted tissues to such an extent as to severely injure them. After heterotransplantation the indirect injurious action of the body fluids, which are unsuitable for the metabolism of the transplanted cells, is more pronounced and leads to the early death of the transplanted cells. We found in the case of skin under these conditions no noticeable activity on the part of the lymphocytes and fibroblasts. J. B. Murphy, however, recently showed through very ingenious experiments that in the case of heterotransplantation also lymphocytes, under certain conditions, may be of importance as a defensive mechanism of the host.

It has likewise been shown by such investigators as Burgess, DaFano, Baeslack, Rous and J. B. Murphy, that in the case of tumors against which an immunity becomes established, lymphocytes sometimes, in conjunction with other leucocytes, play a distinct rôle in the destruction of the tumor tissue. This holds good in the case of tumors already established. If immunity is produced before the transplanted tumor has united with the host tissues, the ingrowth of fibroblasts and blood-vessels into the transplanted tissue may, according to Russel and Woglom (in the case of tumors) and Peyton Rous (in the case of embryonic tissues) be delayed or else diminished in amount. However, even in the latter case the defence of the organism against the foreign tumor cells may principally consist in an attack by lymphocytes and other leucocytes (E. E. Tyzzer).

As the most probable explanation for these phenomena, we have proposed the following theory[6]: The mutual chemical incompatibility of the body fluids of one individual and the tissues of another, which we could especially clearly demonstrate after homoiotransplantation of pigmented skins, leads to changes in the metabolism of the tissues, resulting in the production of homoio- and heterotoxins, which, if they do not exceed a certain strength, disturb the normal functions of the transplanted tissues to some extent without, however, interfering seriously with their life. But the abnormal products formed attract the lymphocytes and in certain cases also other

[6] Leo Loeb, "The Influence of Changes in the Chemical Environment on the Life and Growth of Tissues," *Journal American Medical Association*, vol. 64, February, 1915, p. 726.

leucocytes, and alter the reaction of the fibroblasts, which latter are induced to produce dense fibrous tissue. If the poisons become more active, they may directly injure tissues to such an extent that growth and life become impossible.

These conclusions, as we believe, also throw light on so-called chronic inflammatory processes of various organs where a changed metabolism of the cells, and perhaps also poisons produced by micro-organisms, may induce fibroblasts to form fibrous bands and attract lymphocytes, thus leading to processes of cirrhosis. In a similar way, in the case of tumor immunity, which, for instance (as Clowes and Gaylord have shown), exists in the case of the retrogression of tumors, substances produced as a result of immunization and which circulate in the body fluids alter the metabolism of the tumor cells, which in turn influence the activity of the leucocytes and fibroblasts in a way similar to normal tissues in a strange host. This theory correlates the immunity against tumor and tissue growth with the immunity against certain substances and non-growing foreign cells. We have also in the former case to deal with the production of immune substances, which, however, in the case of homoiotransplantation, are usually not such that they directly destroy the foreign tissues, but merely lead to an alteration of their metabolism and to the production of substances which change the behavior of the host cells. We no longer need to assume a primary tissue alteration following the homoiotransplantation.

It remains for further investigation to decide to what extent the presence of foreign tissue leads to the direct production of what we could call primary homoio- and heterotoxins as the result of the interaction between the preformed constituents of the body-fluids and the foreign cells, and to what extent it leads to the production of secondary homoio- and heterotoxins—the immune substances—as the result of immune reactions. At present it appears probable that both these substances play a rôle. *In vitro* the toxicity of body fluids of foreign species is apparently not very marked, as we, as well as Lambert, found. The toxicity is certainly less than we should expect, considering the fate of tissues after heterotransplantation. We must, however, take into account the fact that the amount of body fluid and especially of toxin acting on the tissue *in vitro,* is extremely small as compared with the quantity acting in the living body, and that this reduction in the quantity of body fluid is very much greater than the reduction in the quantity of tissue.

Furthermore, in the body the fluid in contact with the tissue is constantly renewed and the old fluid is eliminated. *In vitro* the fluid remains relatively constant. There exists also the possibility that the action of the body fluid is a complex one *in vivo* in a way similar to the complex action after homoiotransplantation. In the case of both types of substances (those preformed and those produced through immunization), we are able to point to analogous substances existing elsewhere, namely, the preformed species-specific tissue coagulins, which play a rôle in the blood coagulation, and the secondarily, artificially produced antibodies of various kinds. It also remains further to be determined how far the metabolic products of foreign cells exert a direct influence upon each other and how much of this effect is dependent upon the interaction between cells and foreign body fluids.

In addition to the effect of toxic substances, mere lack of common food-stuffs can also retard tumor growth, as the retarded growth of transplanted tumors in pregnancy and the feeding experiments of Moreschi, Peyton Rous, Beebe, Sweet, Corson White, and Saxon, Robertson and Burnett have shown. Other substances apparently stimulate tumor growth (Robertson and Burnett). Whether an immunity caused through the lack of specific substances—in contradistinction to the common food and growth stuffs of cells—whether, in other words, an athreptic immunity, as Ehrlich called it, exists, however, is very doubtful. Such an athreptic immunity certainly would not explain the phenomena referred to above, as especially the experiments of Uhlenhuth, Haendel and Steffenhagen, Tyzzer and Levin have shown.

In the retarded cancer growth in pregnancy especially we do not have to deal with a scarcity in specific growth substances, particularly in hormones, as Ehrlich supposed, but with a shortage in the ordinary substances required for the building up of cells. On the contrary, it seems to us very probable that certain hormones which circulate during pregnancy may be of advantage to tumor growth, and that these two antagonistic factors—deficiency in ordinary building material and presence of special hormones—may preponderate unequally in different cases and thus the difference in the effects on tumor growth which certain investigators found in pregnancy may be explained.

In connection with the studies in metabolism to which we have just referred, we may look forward to interesting results through further analysis of the chemical constitution of tumor tissues.

I am, however, inclined to regard the differences so far found between normal and tumor cells in a similar light, as differences observed in the case of mitotic division in normal and tumor cells, both probably being the result and not the cause of the changes in the growth energy characteristic of tumor cells.

Having arrived at the end of our survey, we must confess that much remains still to be done before these investigations can in any way be considered near completion. On the other hand, I believe that I have indicated that there are yet other ways open for further attack upon the problems of cancer and tissue growth, and I hope also that I have been able to convey the impression that the work of so many investigators in this field has not been in vain, and that not only this special branch of science has been built up, but that also biology and pathology in general have been stimulated and enriched as the result of their labors.

DEPARTMENT OF COMPARATIVE PATHOLOGY,
WASHINGTON UNIVERSITY.

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## EDITORIAL.

### PROF. SAMUEL P. SADTLER.

The retirement from active service of one who has spent thirty-eight years of his life as a teacher will cause his colleagues of the Faculty and his former students in the Alumni to contemplate in retrospect the progress of the College during these years and his part in the development. When Professor Sadtler succeeded Professor Bridges to the Chair of Chemistry in the Philadelphia College of Pharmacy the time devoted to instruction in this subject consisted of two hours per week, during about five months of the year, to each of the classes. The course consisted of two years, and a perusal of the examination questions as published in this JOURNAL at that time shows that the teaching in fundamental principles was held to be as important as to-day. Indeed, we are prone to conclude that the students of that time were as serious-minded and in after-life attained as great distinction as the graduates of recent years. Of course, the conditions of thirty-five years ago were very different from to-day. The individual counted for more, and there was neither the specialization in the industries and arts nor the combination of capital that there is at the present time.

In 1880, the final examinations in the Philadelphia College of Pharmacy were held from February 28 to March 4. The commencement took place on March 18, and Professor Sadtler was the recipient of a handsome silver tea-set presented to him by the class. From the very first he took a quiet but very deep interest in the College. The Department of Chemistry gradually developed, due largely to his efforts and those of Professor Trimble, until to-day there are courses in chemistry requiring from three to four years of the student's entire time. The graduates in this department usually have been successful, and a number of them occupy positions reflecting credit on themselves and the school. While not actively connected with the laboratory, he has always encouraged practical courses and stimulated students to engage in research work.

Professor Sadtler was made a member of the Publication Committee of the AMERICAN JOURNAL OF PHARMACY in 1895, and has been actively connected as chairman most of this time. Professor Sadtler's fame rests largely on his text-books and his work as an industrial chemist. During the past twenty-five years he has earned a reputation as one of America's foremost chemical experts. For the benefit of the members of the College and the Alumni the main facts connected with Professor Sadtler's career are given elsewhere in this issue.

## THE AGE OF CONSOLIDATION.

As a measure of efficiency there can be nothing but praise for the merger of the University of Pennsylvania Medical School, Jefferson College, and Medico-Chirurgical College under a unified control that will enable far better results to be obtained than under the present system. The consolidation is a perfectly natural one, because it is in line with a country-wide movement to reduce the number of medical colleges and advance the standard of those that remain. It has perhaps not been generally recognized that six institutions for the training of doctors are really more than Philadelphia's share, and that the competition for students has not been a healthy one. There has been a division of energy and resources and all the schools have suffered. The concentration of the strength of three of these rivals into one large and admirably equipped institution cannot fail to be of the greatest benefit to the city as a centre of medical education.

The plan has for its fundamental features the adoption of the elective system in effect at Vienna and Oxford, which permits stu-

dents to decide whose lectures they shall attend on any subject during the term, and the establishment of a post-graduate school at the University to perpetuate the name of the Medico-Chirurgical College. The Jefferson Medical College and University Medical School form a union on a basis of exact equality whereby both institutions and the medical world will, it is declared, be accorded distinct advantages. The united schools will be known as The Medical School of the University of Pennsylvania and the Jefferson Medical College of Philadelphia. The elective system, which is made effective in pursuing studies under the plan, is declared to represent the biggest step looking toward the advancement of the study of medicine that has been made in this country, largely because of its flexibility. It is pointed out that under the system of operation examinations will be held by a commission and the standing of students determined in units, which in effect will put upon the professors the burden of producing results, and will influence higher standards, at the same time giving wider range of opportunity for individual progress. One of the most commendable features of the consolidation is that by which Medico-Chirurgical College, under University control, will be set apart for post-graduate and research work. This is a department in which the divided schools have hitherto been lacking. With a new hospital to replace that which stands on the line of the Parkway, unrivalled opportunities will be afforded for advanced students in this branch of medical training.

The address of Dr. W. W. Keen at the recent Commencement of Jefferson Medical College is deserving of very careful reading by all who are interested in medical education. The distinguished and venerable surgeon, who graduated from Jefferson fifty-four years ago, used his lancet mercilessly in an effort to arouse the medical men and the business men of the city to unite in restoring Philadelphia to her former place of undisputed leadership in medical affairs.

Discussing the union between the Jefferson Medical College and the University of Pennsylvania Medical School, Dr. Keen denied emphatically the argument that the merger would strangle competition between Philadelphia's various medical schools. He insisted that the " real " competition was not between any of the Philadelphia institutions, but that it is " a competition between Philadelphia on the one side, and the schools in Boston, New York, Baltimore, Chicago, St. Louis, and elsewhere on the other." " It is time," said he, " that some one in Philadelphia should speak out boldly and plainly, even

at the risk of adverse criticism. My age, my long service as a teacher, my present detachment from active teaching and determination of policy, would seem to justify my undertaking this frankly unwelcome task." Dr. Keen then went on to show that Philadelphia has fallen far behind other cities named in the comparative rank of its medical schools. He asserted that this decline was due neither to the superior advantages offered by the faculties of schools in other cities, nor to the professional ability of their graduates. Philadelphia's teachers and Philadelphia's medical graduates were just as good as those of any other city, he maintained, citing a long list of distinguished physicians in support of his claim. But in two other respects, he asserted, the number of students and the financial resources of the schools, Philadelphia had fallen lamentably behind other cities.

" In respect to the number of students," he said, " Jefferson is at the very top. In spite of the enormous decrease in the total number of students in the entire United States in the last ten years—amounting to a decrease of forty per cent. or more—and of the increased requirements for admission which the Jefferson has instituted in the session of 1914–15, the Jefferson registered 556 students, the largest number in any American medical school. The union with the University of Pennsylvania will, therefore, bring together the largest and the oldest medical schools in the United States. The next largest school (in Chicago) had 487, including thirty-five women students; the third (New York) had 381; the fourth (New York), 364; the fifth (Baltimore), 361, including thirty-one women; the sixth (Boston), 319; the next the University of Pennsylvania, 276. All the others registered much smaller numbers.

" But when we take a still broader view and compare the relative position of Philadelphia as a medical centre, including all its schools in comparison with all those in the five other principal medical centres just named, the result is far from flattering to Philadelphia. In 1846, seventy years ago, Philadelphia in its three schools had 915 students, and the other five cities had 978 students. Chicago had not then a single student.

" In 1855, sixty-one years ago, Philadelphia's four schools had 1189 students and the other five cities 959. Chicago then had seventy students. In 1903, thirteen years ago, when the total number of students in the United States reached its maximum (27,615), Philadelphia had 2139 students and the other five cities 8782. From the large percentages at the earlier dates Philadelphia had fallen to only

one-fourth of the total number in the other five cities. Chicago had risen to 2476 and New York to 2039, the latter within one hundred of our total number (2139), while Chicago had over 300 more than Philadelphia. In 1915, when the number had fallen to 14,891 students, Philadelphia had 1267, while the other five cities had 6112, giving us one-fifth of the total number in the other five cities. Chicago had 2093 and New York 2041, each exceeding the number in Philadelphia by about 800 students. The contrast between the financial resources of Philadelphia medical schools and those of other American medical centres is a sad record of parsimony here and lavish generosity elsewhere. As nearly as I can estimate, not including state appropriations nor gifts prior to 1910, though these were many and large, the gifts to medical schools and their hospitals in Boston aggregate over $6,500,000. This includes the new Peter Bent Brigham Hospital, but not the splendid new buildings of the Medical School. The New York Schools, excluding Columbia, have received about $8,000,000, while Columbia has an ambitious plan for union with the Presbyterian Hospital. This alone will involve a total expenditure of $16,000,000. Part of this has already been pledged. The rest will follow. The Baltimore schools have received $3,500,000 in gifts which have been published. Other large sums have been paid since and large future plans are in contemplation. In Chicago over $7,000,000 has been given. Very ambitious plans are being considered there also. In St. Louis the gifts to Washington University amount to between $7,000,000 and $8,000,000. Besides this, it has the residuary legatee of two estates, running into the millions. The Rockefeller Institute also in New York has received $12,500,000. Our Philadelphia medical institutions in the same six years have received a little over $4,000,000. True, this in itself is a large sum, but in comparison with the gifts I have just cited, it is wholly inadequate.

"To place Philadelphia in the position she so long occupied we shall run a losing race unless our citizens are aroused by my figures. They must think in millions instead of thousands. They must be not only proud of their heritage, but anxious to see our ancient city restored to the front rank. Civic pride which has been such a magnificent asset to St. Louis—a much smaller city than Philadelphia—should stir the hearts and loosen the purse-strings of our merchants, manufacturers and capitalists. Medical 'Philadelphia To-day,' inadequate as it is, we have with us; Medical 'Philadelphia To-morrow,' we must realize by combined effort, 'a long pull, a strong pull,

and a pull all together.' Herein lies the value of combination of our medical schools and the utilization of all our medical resources. The union of the largest school and the oldest school is, in my judgment, the first and most important step, but far, far from the last. The co-operation of our active state and county medical societies, of the efficient Departments of Health, of the state and city, and, above all, the loyalty and energetic assistance of the whole profession must be mobilized. We should also enlist the energetic City Club and the Chamber of Commerce, not so much for their direct financial help as for their moral support and their influence in creating a sympathetic public opinion."

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## THE PHILADELPHIA COLLEGE OF PHARMACY.

### Ninety-fifth Annual Commencement.

The exercises of Commencement in the Philadelphia College of Pharmacy began with Baccalaureate services at the Church of St. Luke and the Epiphany on Sunday, June 4. The sermon was delivered by Rev. Dr. David M. Steele. The Professors' Banquet to the graduating class was held in the College auditorium on Monday evening, June 5. Alumni Day was Tuesday, June 6. The annual meeting was held in the morning, followed by class day exercises in the afternoon and a reunion banquet at the Hotel Adelphia in the evening.

The Commencement exercises were held on Wednesday evening, June 7, at the American Academy of Music, when the diplomas and prizes were awarded to the members of the graduating class. The opening prayer was made by Rev. Herman S. Cook, and an address was delivered by Rev. John G. Wilson, D.D. The degrees were conferred by President Howard B. French upon the following.

The following are the names of those receiving the degree of Doctor in Pharmacy (P.D.), together with the subjects of their graduating theses:

| Name | Thesis | |
|---|---|---|
| Alff, Rudolph Eric | Bacteriology as an Asset to the Pharmacist | Wisconsin |
| Ankerbrand, Walter Frank | American Ginseng | Pennsylvania |
| Beecher, Lew Wallace | Photographic Supplies, A Valuable Adjunct to Pharmacy | Pennsylvania |
| Belles, Arthur Hartman | Ipecacuanha | Pennsylvania |
| Bernstein, Miss Ada Malvina | Italian Drug Store in an American City | Pennsylvania |

| Name | Thesis | |
|---|---|---|
| Blanco, Ramon Mas | Cork | Cuba |
| Blaustein, Louis Nathan | Bees Wax | Pennsylvania |
| Blum, Charles Julius | Extraction of Asparagin from Althaea | Pennsylvania |
| Bongiovanni, Joseph Nathaniel. | Pepsin | Italy |
| Bosserman, Charles | Manna | Pennsylvania |
| Brendle, Lester Yoder | Urinalysis | Pennsylvania |
| Buoymaster, Paul | Limestone and Lime | Pennsylvania |
| Carn, Fred LeRoy | Embalming and Embalming Fluids | Pennsylvania |
| Cash, Artemus Bogan | Bile and the Bile Salts | No. Carolina |
| Collins, John Edward | Brass | Pennsylvania |
| Davis, Ellerslie Wallace | Castor-Jell | Pennsylvania |
| Dawe, William John | Limestone | Pennsylvania |
| Depew, Samuel Harry, Jr. | Liquefaction of Gases | Pennsylvania |
| Dilatush, Owen Philip Eaches. | The Pineal Gland | New Jersey |
| Durand, Chalmer John | Estimation of Sulphur in Pyrites. | Pennsylvania |
| Eisman, Charles Kolman | Hamamelis | Pennsylvania |
| Escanaverino, Miss Louisa Lutgarda | Anacardium Occidentale | Cuba |
| Escanaverino, Miss Maria Dolores | Theobroma Cacao | Cuba |
| Ferko, Joseph Aloysius | Vanilla and Its Extract | Pennsylvania |
| Fitzkee, Adam Hastings | Disinfectants and Disinfection | Pennsylvania |
| Gilfillan, James Walls, Jr. | Emetine | Maine |
| Goldblum, Adolph Addie | Peroxide of Hydrogen | Pennsylvania |
| Good, Jacob Edison | Tooth Powders | Pennsylvania |
| Gottshall, Earl Stouffer | Oleum Arachidis | Pennsylvania |
| Graham, John Russell | Liquor Antisepticus | Pennsylvania |
| Green, Raymond | Tinctura Iodi | Pennsylvania |
| Greenleaf, Harry Raymond | The Cohesion Figures of True and Synthetic Volatile Oils | Pennsylvania |
| Guarini, Joseph Raymond | Nitric Acid | Pennsylvania |
| Guest, Warren Rogers | The Manufacture of Gun Powder. | New Jersey |
| Gunn, John Jay | Household Disinfection | Pennsylvania |
| Heiges, George Leonard | Glass, Ancient and Modern | Pennsylvania |
| Heinle, Charles Jacob, P. C. | Paper | Pennsylvania |
| Hendrie, William | Acetylene | Pennsylvania |
| Hill, Clayton Brooks | Paper Manufacture | Pennsylvania |
| Hirzel, George Edgar | Emetine | Pennsylvania |
| Hughes, Edward James | Colloids and Colloidal Solutions | Pennsylvania |
| Ibach, William Henry, Jr. | Cellulose and Its Uses | Pennsylvania |
| James, Rienzi | Soaps | Pennsylvania |
| Karnauskas, Miss Agatha | Store Service | New York |
| Keefer, Norman David | Colloidal Suspensoids | Pennsylvania |
| Keely, Robert Russell | The Harrison Act | Pennsylvania |
| Kindt, Samuel Peter | Cork, Its Origin and Uses | Pennsylvania |

| Name | Thesis | |
|---|---|---|
| Korncavitz, Frank Stanley | Liquor Picis Carbonis | Pennsylvania |
| Kurtz, John Rabold | Ammonium Carbonate | Pennsylvania |
| Lasley, Matthew Ivey | Sodium Bromide | No. Carolina |
| Lax, Isadore | Acidum Hydrochloricum and Acidum Hydrochloricum Dilutum | Pennsylvania |
| LeBar, John Amzi | Dialysis and Diolyzed Iron | Pennsylvania |
| Lehr, Irvin Elias | Pyrethrum | Pennsylvania |
| Lerner, Albert | Cacodylic Acid | Pennsylvania |
| Levy, Robert Allen, P. C. | The Venereal Diseases and Their Relation to Public Health | Pennsylvania |
| Lindenbaum, Isadore Joseph | Monobasic Sodium Phosphate | Pennsylvania |
| Lischer, Henry | Action of Free Iodine on the Upper Air Passages | Pennsylvania |
| Lohrman, Leroy O. | Coca | Pennsylvania |
| Lounsbury, Harry | Creosote Water | New Jersey |
| McAleer, Harold | Insecticides and Fungicides | New Jersey |
| McGinnis, John Frederick | Glycyrrhiza | Pennsylvania |
| Mallard, Oscar Paul | Acidum Hydrochloricum | No. Carolina |
| Martin, John Albert | Citric Acid by Fermentation | Colorado |
| Miller, Clark McCord | The Efficiency of Label Pastes | Pennsylvania |
| Miller, Edward Paul | Enteric Pills and Capsules | Pennsylvania |
| Miller, Robert Jacob | Sterilization of Tooth Brushes and Eye Droppers | Pennsylvania |
| Mouer, Clayton Henry | Magma Magnesiæ | Pennsylvania |
| O'Neill, Vincent Patrick | Drug Store Advertising | Pennsylvania |
| Packer, Emmett Edward | Citrus Trifoliata | Pennsylvania |
| Pascoe, John Gwinner | Glycerin | Pennsylvania |
| Paul, Preston Arlington | The Making of Rubber Goods | Pennsylvania |
| Perrine, Norman, P. C. | Crystallography | New Jersey |
| Peters, Howard Lewis | Modern Hard Soaps | Pennsylvania |
| Piekarski, Joseph William | Lime Water U. S. P. | Pennsylvania |
| Porr, John Wolf | Colleges of Pharmacy in the United States | Pennsylvania |
| Resser, Alpheus William | The Assay of Lime Water | Pennsylvania |
| Rhoads, Paul Edward | Magma Magnesiæ | Pennsylvania |
| Rodgers, Raymond H., P. C. | Fluidglycerates | Pennsylvania |
| Rovner, Arthur | Essence of Peppermint | New Jersey |
| Ryan, Thomas A., P. C. | Adeps Bezoinatus | Pennsylvania |
| Sanchez, Felix Enrique Mestril | Tobacco | Cuba |
| Sarlo, Joseph | Vanilla | Pennsylvania |
| Scheible, Edmund Morris | Solubility of Sulphur in Carbon Disulphide | Pennsylvania |
| Schlegel, Lawrence Brown | Phenolphthalein and Its Uses | Pennsylvania |
| Searight, John Woodburn | Ergot and Its Uses | Pennsylvania |
| Seitzinger, Robert Lawrence | Saturated Solutions | Pennsylvania |

| Name | Thesis | |
|---|---|---|
| Selim, Aly | Carcadiah or Abutilon | Egypt |
| Shaffer, James Walter | Hydrastis Canadensis | Pennsylvania |
| Showers, Guy Warren | Chinese Wood-Oil | Pennsylvania |
| Smith, Dole McClure | Prescription Dispensing | Ohio |
| Smith, William George | Salol Coating of Pills | Pennsylvania |
| Sonne, Ernest Harley | Iodine Petroxolin | Pennsylvania |
| Steel, Max Wensel | Acacia and the Official Mucilage | Pennsylvania |
| Stein, Abraham Mordecai | Calamus | New York |
| Steltzer, Lewis Gustave | Thermalite | Pennsylvania |
| Stokely, Harvey Venton | The Manufacture of White Lead | Ohio |
| Straup, John Wesley | Solidified Alcohol | Pennsylvania |
| Stuart, James Earle | An Intestinal Lubricant | Pennsylvania |
| Suter, Lester Ambrose | Potassii Bitartras | Pennsylvania |
| Tagg, Norman Harvey | Drug Store Cleanliness | Pennsylvania |
| Thornton, Harry Carl | Liquor Alumni Acetatis Crudus "Burrow's Solution" | Pennsylvania |
| Togans, James Albert, Ph.G. | The Germicidal Power of Emetine and the Alcresta Ipecac | Pennsylvania |
| Tucker, Oscar George | Rheum | Pennsylvania |
| Vandegrift, Harry Umsted | Essence of Pepsin | Pennsylvania |
| Wallace, William Alexander | Plant Hairs and Their Importance | Pennsylvania |
| Weatherford, Boyd | Ichthyol and Its Substitution Compounds | Kentucky |
| Webb, Harry Cornelius | Herbs | Pennsylvania |
| Weeks, Kenneth | The Assay of Milk of Magnesia | New Jersey |
| Weidler, Walter Franklin | Liquor Plumbi Subacetatis | Pennsylvania |
| Weidner, Elmer Milton | The Assay of Aromatic Spirit of Ammonia | Pennsylvania |
| Wells, Walter Neff | Show Card Writing and Window Decoration | New Jersey |
| Werkheiser, Harold E., P. C. | Paraffin | Pennsylvania |
| Werntz, Cecil Semmons | Drug Store Side Lines | Pennsylvania |
| Wexlar, Benjamin J. | Cacao Butter and Chocolate | Pennsylvania |
| Whelan, Walter | Turpentine | Wales |
| White, Hobart Pryde | Hyoscyamus | Pennsylvania |
| Whitesell, Elwood E. | The Extraction and Analysis of Molasses from Cane Sugar | Pennsylvania |
| Weiser, John William, Ph.G. | Own Preparation Plan | New York |
| Willard, Miss Elizabeth May | Father Time and Pharmacy | New Jersey |
| Wolf, Clarence Melvin | Citric Acid and Citrates | Pennsylvania |

The following are the names of those graduates who received the degree of Pharmaceutical Chemist (P.C.), together with the subject of their theses:

| Name | Thesis | |
|---|---|---|
| Cravens, John Coldsmith, Jr. | Castor-Jell | Pennsylvania |
| Ehman, Karl Francis | Glycyrrhizin | Pennsylvania |
| Grandy, Seth Parker | Influenza | Pennsylvania |
| Helweg, Lawrence William | Cocoanut Oil | New Jersey |
| Kalusdian, Vartan Mardiros | Perfume and Its Manufacture | Armenia |
| King, Jacob Harris | Filter Paper | Pennsylvania |
| Lenninger, Clifford | Tincture of Strophanthus | Wyoming |
| Luther, Maurice Augustine | Mescal | Pennsylvania |
| McGarrity, Miss Florence Raphael M. | Advertising | Pennsylvania |
| Stikarofsky, Albin | Chelidonium | Austria |
| Waters, Cyrus Albert | Syrupus Ferri Iodidi | Pennsylvania |

Certificates of Proficiency in chemistry were awarded the following:

Herbert Calvin Brightbill, Sylvan L. Foster, P.D., Louis J. Kleinfeld, Howard J. Koch, P.D., Chester L. Masser, John J. Over, Robert Rowen, Max M. Waxman, and George W. Tucker.

A Certificate of Proficiency in the Food and Drug Course was awarded to Louis G. Linford, Ph.G.

Certificates in Bacteriology were awarded to the following:

Miss Silvia C. Alacan, P.D., Rudolph Eric Alff, Ramon Mas Blanco, Charles Bosserman, Parker B. Creep, P.D., Owen Philip Eaches Dilatush, Andrew C. Fayko, Seth Parker Grandy, Vincent Allen Heinle, Joseph A. Hilton, Leo J. McCorriston, Chester Luther Masser, Robert Rowen, Felix Enrique Mestril Sanchez, Jr., Mrs. Mignon Gray Simonin, Dole McClure Smith, Miss Maud Sollenberger, P.D., Mrs. Sadie Swyers, Boyd Weatherford, John W. Wieser, and David B. Witman, P.D.

A Certificate in Analysis of Agricultural Products was awarded to Carlos Marie Aguiar, P.D.

### Award of Prizes.

Presentation of the Martin Cup to the Graduating Class of 1916.

Presentation of "The Graduate 1913" Cup to the Ph.G. Class of 1917.

The grade of Distinguished was attained by Edward J. Hughes and William A. Wallace.

The grade of Meritorious was merited by: Rudolph E. Alff, Luisa L. Escanaverino, Maria D. Escanaverino, Norman D. Keefer, John A. Martin, Ernest H. Sonne, and Albin Stikarofsky.

The William B. Webb Memorial Prize, a gold medal and certificate, offered for the highest general average in the branches of Committee, Operative Pharmacy, and Specimens, was awarded to Edward J. Hughes, the presentation being made by Dr. Adolph W. Miller. The following graduates received honorable mention in connection therewith: Ernest H. Sonne, William A. Wallace, and Elizabeth M. Willard.

The Chemistry Prize, $25, offered by Prof. Samuel P. Sadtler, for knowledge of Quantitative Chemical Analysis, was awarded to Guy W. Showers.

The Materia Medica Prize, $25, offered by Prof. Clement B. Lowe, for the best examination in Materia Medica, and in recognition of Materia Medica Specimens with a meritorious thesis, was awarded to Luisa L. Escanaverino. The following graduates received honorable mention: Maria D. Escanaverino, Edward J. Hughes, Ernest H. Sonne, and William A. Wallace.

The Microscopical Research Prize, a compound microscope, offered by Prof. Henry Kraemer, for the most meritorious thesis involving original Microscopic work, was awarded to John A. Martin. The following graduates received honorable mention: Luisa L. Escanaverino, Maria D. Escanaverino, Felix E. Sanchez, Albin Stikarofsky, and William A. Wallace.

The Analytical Chemistry Prize, $25, offered by Prof. Frank X. Moerk, for the best work in Qualitative and Quantitative Analysis, was awarded to Maria D. Escanaverino. The following graduates received honorable mention in connection therewith: Luisa L. Escanaverino, and William A. Wallace.

The Operative Pharmacy Prize, $20 in gold, offered by Prof. Joseph P. Remington, for the best examination in Operative Pharmacy, was awarded to John W. Straup. The following students merited honorable mention: John E. Collins, Chalmer J. Durand, Adam H. Fitzkee, John R. Graham, Edward J. Hughes, Oscar P. Mallard, John A. Martin, John W. Porr, Albin Stikarofsky, Lester A. Suter, and William A. Wallace.

The Maisch Botany Prize, $20 in gold, offered by Mr. Joseph Jacobs, of Atlanta, Ga., for the best Herbarium Collection of Plants, was awarded to William A. Wallace, the presentation being made by George M. Beringer, chairman of the Board of Trustees.

The Mahlon N. Kline Theoretical Pharmacy Prize, a Troemner agate prescription balance, for the best examination in Theory and

Practice of Pharmacy, was awarded to William A. Wallace, the presentation being made by Clarence M. Kline. The following students merited honorable mention in connection with this prize: Rudolph E. Alff, Luisa L. Escanaverino, Maria D. Escanaverino, John R. Graham, Edward J. Hughes, Norman D. Keefer, and John A. Martin.

The Commercial Pharmacy Prize, $20 in gold, offered by Prof. Joseph P. Remington to the graduate who passed the best examination in Commercial Pharmacy at the final examination for the degree, was awarded to John R. Graham, the presentation being made by Prof. Cook. The following students received honorable mention: Joseph A. Ferko, Edward J. Hughes, Maurice A. Luther, Howard L. Peters, Ernest H. Sonne, Albin Stikarofsky, William A. Wallace, Elizabeth M. Willard, and Clarence M. Wolf.

The Instructors' Prize, $20, offered by the instructors of the College for the highest term average in the branches of Pharmacy, Chemistry, and Materia Medica, was awarded to Maria D. Escanaverino, the presentation being made by Professor Stroup. The following students received honorable mention: Luisa L. Escanaverino, Edward J. Hughes, William A. Wallace, and Elmer M. Weidner.

The Pharmacy Review Prize, one year's membership in the American Pharmaceutical Association, offered by Prof. Charles H. LaWall, for the best term work in Theory and Practice of Pharmacy, was awarded to William A. Wallace. The following received honorable mention: Rudolph E. Alff, Maria D. Escanaverino, Joseph A. Ferko, Edward J. Hughes, and John R. Kurtz.

The Kappa Psi Fraternity Prize, a gold medal, offered by the Eta Chapter of the Kappa Psi Fraternity to the graduate making the highest general average during the senior year at the College, was awarded to Edward J. Hughes, the presentation being made by Prof. Roddy. The following students merited honorable mention: Rudolph E. Alff, Maria D. Escanaverino, and William A. Wallace.

The Special Lecture Report Prize, $10 in gold, awarded for the best written reports of the series of special lectures held under the auspices of the College, session 1915–1916, was awarded to Albin Stikarofsky, the presentation being made by Mr. Samuel C. Henry.

The Col. H. C. Demming Prize, a $50 Oriental ruby, for the best and most satisfactory advancement during the College year 1915–1916, was awarded to Max Wensel Steel, the presentation being made by Prof. Remington.

## FIFTIETH ANNIVERSARY ALUMNI CELEBRATION, P. C. P.

At a recent meeting of the committees representing the Board of Trustees of the College and the Alumni Association, it was decided that the 50th Anniversary Alumni Celebration of the Philadelphia College of Pharmacy take place at the time of the A. Ph. A. meeting next September. There will be two separate functions.

1. The Fiftieth Anniversary Alumni Reunion and Testimonial Dinner to Professor Sadtler. This function will be held at Atlantic City during the week beginning September 4.

2. An exhibition at the Philadelphia College of Pharmacy illustrating the progress in pharmacy during the past fifty years.

These events promise to be of great importance and will interest not only the Alumni of the Philadelphia College of Pharmacy but those pharmacists and their friends who will attend the Atlantic City meeting of the American Pharmaceutical Association. The Reunion Dinner, which will take the form of a tribute to Professor Sadtler, who is retiring after more than thirty-five years of active service in the Philadelphia College of Pharmacy, will be attended by America's foremost pharmacists and chemists.

The Historical Exhibition will be held at the Philadelphia College of Pharmacy, and will be open from August 28 until September 10. The spacious Museum will be entirely devoted to a college exhibit of apparatus, specimens, books, and portraits. The lecture-rooms and the halls will contain the exhibits of manufacturers and others. It is anticipated that there will be a large display of rare chemicals and preparations, apparatus, fixtures, old drugs, curios, books, diplomas, certificates, medals, manuscripts, letters, lecture tickets and portraits of distinguished pharmacists. All who can in any way contribute to the success of this exhibition are earnestly requested to loan such material of this kind as they may have, which will be protected with duplicate checks so that there will be no confusion or loss on the part of those who will kindly loan the material.

As the time is relatively short for the final arrangements of the exhibition, it is very much desired that those wishing to contribute to the historical exhibit will promptly communicate with the committee.

HOWARD B. FRENCH,
*Chairman.*

HENRY KRAEMER,
*Secretary.*